Contraception Update for the Dermatologist

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Professor, University of Pittsburgh School of Medicine
Department of Dermatology

UNIVERSITY OF PITTSBURGH
Conflicts of Interest

• None
Pregnancy on isotretinoin over time


Highest rate of Pregnancy among women 20-29

Start of iPledge (2006)

**No. of pregnancies**
- 7
- 83
- 62
- 85
- 129
- 154
- 382
- 519
- 672
- 768
- 525
- 719
- 388
- 471
- 265
- 247
- 310
- 243
- 243
- 218
- 250

**No. of pregnancy-related outcomes**
- Pregnancy on contraceptives:
  - 1
  - 3
  - 0
  - 1
  - 1
  - 3
  - 2
  - 6
  - 5
  - 35
  - 51
  - 64
  - 43
  - 13
  - 16
  - 5
  - 8
  - 9
  - 10
  - 1
  - 1
- Therapeutic abortion:
  - 0
  - 0
  - 0
  - 0
  - 0
  - 6
  - 104
  - 92
  - 152
  - 148
  - 247
  - 52
  - 123
  - 33
  - 16
  - 25
  - 50
  - 52
  - 31
  - 32
- Spontaneous abortion:
  - 0
  - 54
  - 9
  - 13
  - 17
  - 32
  - 24
  - 49
  - 66
  - 92
  - 63
  - 44
  - 28
  - 28
  - 27
  - 26
  - 34
  - 31
  - 36
  - 30
  - 30
- Fetal defect:
  - 3
  - 13
  - 20
  - 34
  - 30
  - 26
  - 19
  - 8
  - 17
  - 12
  - 3
  - 9
  - 2
  - 2
  - 1
  - 3
  - 1
  - 4
  - 0
  - 2
  - 1
Contraception, Pregnancy, and iPledge

• Most common contraception chosen by women on iPledge
  • Combined oral contraceptives (COC) + condoms

• Most common contraception chosen by women who become pregnant on iPledge
  • COC + Condoms
  • Abstinence
Anonymous survey of WOCBP currently taking isotretinoin

- 4/21 (19%) patients who chose abstinence as primary method became sexually active during isotretinoin therapy
- 12 women had sex with 0 or 1 form of contraception
  - 10 of whom did not use condoms
  - 1 used no protection
- 39% of pill users missed one or more pills in the previous month

<table>
<thead>
<tr>
<th>Metric</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Used 2 approved forms of contraception during last sexual encounter on isotretinoin</td>
<td>31 (79)</td>
</tr>
<tr>
<td>Had completely unprotected vaginal intercourse since starting isotretinoin</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Had vaginal intercourse using ≤ 1 approved forms of birth control since starting isotretinoin</td>
<td>12 (31)</td>
</tr>
<tr>
<td>No. of oral contraceptives missed or taken late in last month*</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>11 (61)</td>
</tr>
<tr>
<td>1</td>
<td>4 (22)</td>
</tr>
<tr>
<td>2</td>
<td>1 (6)</td>
</tr>
<tr>
<td>3-4</td>
<td>2 (11)</td>
</tr>
<tr>
<td>≥ 5</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Of 18 sexually active women who pledged to use oral contraceptive pills for iPLEDGE.
Counseling women on contraception options
Table 2. Baseline Knowledge of the Typical Effectiveness of Available Contraceptives

<table>
<thead>
<tr>
<th>Contraceptive</th>
<th>Overestimated Typical Effectiveness</th>
<th>Underestimated Typical Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subdermal implant</td>
<td>NA</td>
<td>55</td>
</tr>
<tr>
<td>IUD</td>
<td>NA</td>
<td>39</td>
</tr>
<tr>
<td>Injection</td>
<td>57</td>
<td>6</td>
</tr>
<tr>
<td>Ring</td>
<td>25</td>
<td>7</td>
</tr>
<tr>
<td>Patch</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Pills Condom</td>
<td>51</td>
<td>8</td>
</tr>
<tr>
<td>Withdrawal</td>
<td>13</td>
<td>NA</td>
</tr>
</tbody>
</table>

Table 3. Change in Contraceptive Knowledge Following Review of Information Sheet

<table>
<thead>
<tr>
<th>Contraceptive</th>
<th>Improvement Among Women Who Initially Inaccurately Identified the Typical Effectiveness of a Method, Proportion (%)</th>
<th>Participants, %</th>
<th>Pretest Correct</th>
<th>Posttest Correct</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subdermal implant</td>
<td>35/55 (64)</td>
<td>45</td>
<td>78</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>IUD</td>
<td>26/39 (67)</td>
<td>61</td>
<td>83</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Injection</td>
<td>23/72 (32)</td>
<td>28</td>
<td>44</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Ring</td>
<td>20/40 (50)</td>
<td>60</td>
<td>69</td>
<td>.18</td>
<td></td>
</tr>
<tr>
<td>Patch</td>
<td>31/50 (62)</td>
<td>50</td>
<td>71</td>
<td>.002</td>
<td></td>
</tr>
<tr>
<td>Pills Condom</td>
<td>28/59 (47)</td>
<td>41</td>
<td>65</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Withdrawal</td>
<td>22/75 (29)</td>
<td>25</td>
<td>45</td>
<td>.003</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18/26 (69)</td>
<td>74</td>
<td>90</td>
<td>.003</td>
<td></td>
</tr>
<tr>
<td>Contraceptive</td>
<td>Conclusions</td>
<td></td>
<td></td>
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<tr>
<td>-----------------------</td>
<td>-----------------------------------------------------------------------------</td>
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</tbody>
</table>
| Combined oral contraceptives | *Improves acne* (strong evidence)  
COCs have an overall net antiandrogenic effect due to the combined effects of ethinylestradiol and progestin, with few therapeutic differences between the various COC options [7, 9, 11–13, 130–132]  
The US FDA has approved four COCs for the treatment of acne:  
Ethinylestradiol/drospirenone  
Ethinylestradiol/norgestimate  
Ethinylestradiol/drospirenone/levomefolate  
Ethinylestradiol/norethindrone acetate/ferrous fumarate |
| Vaginal ring           | *Improves acne* (moderate evidence)  
On average, vaginal ring users reported an improvement in acne, with even fewer reports of worsening acne than COCs [13, 18–20] |
| Skin patch             | *Improves acne* (limited evidence)  
Reduction in acne reported in 33% of users following patch initiation, and commonly reported in several case series [15–17] |
| Hormonal IUD           | *Causes acne* (moderate evidence)  
No RCTs have directly evaluated IUDs on acne vulgaris. Several studies have noted the worsening of acne lesions and acne is one of the most common causes of IUD discontinuation [13, 22–28] |
| Subdermal implant      | *Causes acne* (moderate evidence)  
One of the most common adverse events and reasons for discontinuation, with 3–27% of patients reporting acne in clinical trials [13, 29–33] |
| Depot injection        | *Causes acne* (moderate evidence)  
Acne has frequently been reported as a minor adverse effect among users [13, 34–40] |

*COCs* combined oral contraceptives, *RCTs* randomized controlled trials, *IUD* intrauterine device
Simplifying contraception requirements for iPLEDGE: A decision analysis

John S. Barbieri, MD, MBA, Andrea H. Roe, MD, MPH, and Arash Mostaghimi, MD, MPA, MPH
Philadelphia, Pennsylvania; and Boston, Massachusetts

Table I. Contraceptive effectiveness during within first 6 months of (typical) use

<table>
<thead>
<tr>
<th>Variable</th>
<th>COC, hormonal patch/ring, %</th>
<th>Barrier methods, %</th>
<th>Fertility awareness, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tier 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subdermal hormonal implant</td>
<td>99.975</td>
<td>99.998</td>
<td>99.996</td>
</tr>
<tr>
<td>Permanent surgical contraception (ie, vasectomy)</td>
<td>99.925</td>
<td>99.993</td>
<td>99.987</td>
</tr>
<tr>
<td>Permanent surgical contraception (ie, tubal ligation)</td>
<td>99.750</td>
<td>99.978</td>
<td>99.955</td>
</tr>
<tr>
<td>Nonhormonal IUD</td>
<td>99.600</td>
<td>99.964</td>
<td>99.928</td>
</tr>
<tr>
<td>Tier 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMPA injection</td>
<td>97.000</td>
<td>-</td>
<td>99.460</td>
</tr>
<tr>
<td>Combined hormonal pill/patch/ring</td>
<td>95.500</td>
<td>-</td>
<td>99.190</td>
</tr>
<tr>
<td>Tier 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barrier methods (condoms, sponge, diaphragm)</td>
<td>91.000</td>
<td>99.190</td>
<td>-</td>
</tr>
<tr>
<td>Fertility awareness-based methods</td>
<td>88.000</td>
<td>98.920</td>
<td>97.840</td>
</tr>
<tr>
<td>Abstinence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abstinence (twice weekly model)</td>
<td>97.571</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Abstinence (weekly model)</td>
<td>97.979</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Abstinence (monthly model)</td>
<td>99.201</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Abstinence (yearly model)</td>
<td>99.891</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
We pledge to change iPledge! Progress by AADA!

• Request for reclassification as patients who cannot become pregnant has been granted and is underway (expected later this year)

• Request to reduce attestation frequency for patients who cannot become pregnant has gained traction with the FDA and the sponsors.
  • the FDA informed the iPledge sponsors that it is willing to review a proposal to reduce the attestation policy
  • after the reclassification has been approved and launched, the sponsors would like to meet with the AADA to discuss the proposal in further detail, prior to their meeting with the FDA
  • Sponsors estimate they would be ready for this meeting in early Q1 of 2022.
Contraception: Beyond isotretinoin

• Thalidomide
• Mycophenolate mofetil / mycophenolic acid
• Acitretin
Key Points:

- Providers must enroll in Thalomid REMS program and agree to follow requirements ([CelgeneRiskManagement.com](http://CelgeneRiskManagement.com))
- For females of reproductive potential, need 2 negative pregnancy tests. One test must be obtained 10 to 14 days and one test within 24 hours prior to writing an initial prescription. 2 forms of contraception (similar to isotretinoin).
- Monthly confidential surveys must be completed by provider and patient (except women NOT of childbearing potential)
- Must counsel no blood or sperm donation, minimize drug handling, return unused product to provider
- Men must use a condom if sexually active with person who is or can become pregnant
Effectiveness of Risk Evaluation and Mitigation Strategies (REMS) for Lenalidomide and Thalidomide: Patient Comprehension and Knowledge Retention

Nancy A. Brandenburg1 · Robert Bwire1 · John Freeman1 · Florence Houn1 · Paul Sheehan1 · Jerome B. Zeldis1

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Initial surveys</th>
<th>Initial birth control (%)</th>
<th>Follow-up surveys</th>
<th>Follow-up birth control compliance (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females of reproductive potential</td>
<td>233</td>
<td>219 (94.0)</td>
<td>147</td>
<td>134 (91.2)</td>
</tr>
<tr>
<td>Males (adult and child)</td>
<td>1532</td>
<td>1480 (96.6)</td>
<td>1443</td>
<td>1399 (97.0)</td>
</tr>
<tr>
<td>Total</td>
<td>1765</td>
<td>1699 (96.3)</td>
<td>1590</td>
<td>1533 (96.4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Message</th>
<th>Females of reproductive potential</th>
<th>Adult females not of reproductive potential</th>
<th>Males aged ≥ 18 years</th>
<th>Males aged 12–17 years</th>
<th>Children aged &lt; 12 years</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total surveyed</td>
<td>147</td>
<td>979</td>
<td>1441</td>
<td>2</td>
<td>7</td>
<td>2576</td>
</tr>
<tr>
<td>Product can cause birth defects</td>
<td>146</td>
<td>958</td>
<td>1417</td>
<td>2</td>
<td>7</td>
<td>2530 (98.2)</td>
</tr>
<tr>
<td>Sharing product with others can be dangerous</td>
<td>146</td>
<td>969</td>
<td>1417</td>
<td>2</td>
<td>7</td>
<td>2541 (98.6)</td>
</tr>
<tr>
<td>Women should not get pregnant while taking product</td>
<td>144</td>
<td>958</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1102 (97.9)</td>
</tr>
<tr>
<td>Men should use condoms while on product if they are sexually active with a woman who is able to become pregnant</td>
<td>–</td>
<td>–</td>
<td>1418</td>
<td>2</td>
<td>–</td>
<td>1420 (98.4)</td>
</tr>
<tr>
<td>Unused product needs to be returned</td>
<td>129</td>
<td>866</td>
<td>1239</td>
<td>2</td>
<td>7</td>
<td>2243 (87.1)</td>
</tr>
</tbody>
</table>
Mycophenolate mofetil / mycophenolic acid

National Transplantation Pregnancy Registry data: prospective cases of 33 pregnancies in 24 female transplant patients taking mycophenolate

- 15 spontaneous abortions (45%)
- 18 live-born infants
- Four of the 18 live-born infants had birth defects (22%).
  - Congenital malformations of external ear, cleft lip and palate
  - Anomalies of the distal limbs, heart, esophagus, kidney, and nervous system
### Acceptable Birth Control Options

Talk with your doctor and pick from the following birth control options during treatment with mycophenolate.

**Option 1 | Use Method Alone**
- Pick one item from (A)
  - **Most effective**: Less than 1 pregnancy per 100 women in one year

- **A**
  - Intrauterine Device (IUD)
  - Tubal Sterilization
  - Vasectomy

**Option 2 | Use Hormone & Barrier**
- Pick one item from (B) and one item from (C1) or (C2) shown below
  - 4-7 pregnancies per 100 women in one year

- **B**
  - Progestosterone Only Injection
  - Birth Control Pill
  - Birth Control (Progestosterone) Patch
  - Vaginal Ring
  - Progestosterone Only Implant

**Option 3 | Use Two Barriers**
- Pick one item from (C1) and one from (C2)
  - **Least effective**: 13 or more pregnancies per 100 women in one year

- **C**
  - Female Condom
  - Male Condom
  - Female Diaphragm with Spermicide
  - Female Birth Control Sponge
  - Cervical Cap with Spermicide

### What is my role in the Mycophenolate REMS?

1. Document your training in the Mycophenolate REMS
2. Educate Females of Reproductive Potential on the increased risks of mycophenolate
3. Check pregnancy status of patients
4. Reassess treatment options for patients who are considering becoming pregnant
5. Report any pregnancies to the Mycophenolate Pregnancy Registry
**SORIATANE**
(acitretin) Capsules

**SORIATANE SCHEDULE FOR PREGNANCY PREVENTION & SAFE PREGNANCY PLANNING**

<table>
<thead>
<tr>
<th></th>
<th>1 MONTH BEFORE TREATMENT</th>
<th>BEFORE TREATMENT</th>
<th>DURING TREATMENT WITH SORIATANE</th>
<th>2 MONTHS AFTER TREATMENT</th>
<th>3 YEARS AFTER TREATMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 FORMS OF BIRTH CONTROL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 NEGATIVE PREGNANCY TESTS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ONGOING PREGNANCY TESTS</td>
<td>Each month before receiving prescription and every 3 months for 3 years after stopping treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO ALCOHOL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NO BLOOD DONATION</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SIGN INFORMED CONSENT</td>
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</tbody>
</table>
PATIENT SELF-EVALUATION

Now that you have read the Do Your P.A.R.T.™ brochure and talked with your doctor about SORIATANE and its risks, please use this self-evaluation exercise to test your understanding of some of the most important points.

Please choose the best answer for each of the following 7 questions.

1. Treatment with SORIATANE requires prevention of pregnancy because:
   a. Severe psoriasis may get worse after pregnancy
   b. SORIATANE can cause birth defects
   c. Psoriasis is more likely in children of psoriasis patients
   d. None of the above

2. Before starting treatment with SORIATANE, it is important to be certain I am not pregnant. To be certain, I must:
   a. Test my urine at home with 2 pregnancy test kits
   b. Have my doctor order 2 pregnancy tests, 2 weeks apart
   c. Have my doctor do a screening test for pregnancy when we decide to treat me with SORIATANE, and then test for pregnancy again during the first 5 days of my period (or at least 11 days after the last time I had sex without birth control) to confirm I am not pregnant
   d. Not have sex for one month

3. I must start using 2 effective forms of birth control:
   a. At least 1 month before starting SORIATANE
   b. At the time I take the first dose of SORIATANE
   c. After my period ends
   d. Now

4. I must continue using 2 effective forms of birth control:
   a. As long as I continue to take SORIATANE
   b. For 1 year after I stop taking SORIATANE
   c. For 3 years after I stop taking SORIATANE
   d. Until menopause

5. True or False? (circle one) T F
   It is important to avoid alcohol while taking SORIATANE and for 2 months after stopping SORIATANE because alcohol can change SORIATANE into another substance that may also cause birth defects, and that lasts in the body for even longer than SORIATANE.

6. True or False? (circle one) T F
   A female patient with severe psoriasis has used birth control pills for 7 years after her last child was born and they have worked just fine. She still needs to add a second method of birth control before starting treatment with SORIATANE.

7. True or False? (circle one) T F
   Avoiding pregnancy during and after treatment with SORIATANE is equally the responsibility of my doctor, my partner, and me.
What about men?

• There is no risk to men conceiving while on isotretinoin
• Men do need to be counseled about:
  • risk of sharing medications with people of child-bearing potential
• Restrictions on blood donation:  
  • 1 mo for isotretinoin
  • 1 mo for thalidomide
  • 3 years for acitretin
• Men do need to be counseled about risks associated with
  • MTX: DNA damage to sperm
  • Thalidomide: exposure via semen to people who are or can become pregnant
Human genital differentiation occurs at week 6 – 14

In humans, 5 males were born to mothers with renal disease who were treated with spironolactone before and during their pregnancies. No evidence of feminization despite exposure to doses as high as 400 mg a day
• Improved facial and truncal acne
• Median drug survival = 327 days
  • Most common reason to stop was acne clearance
• 23% of discontinuations were due to adverse effects (15 non-menstrual, 6 menstrual)
  • menstrual adverse effects significantly less common among those using combined oral contraception (OR, 0.23)
• No contraindications (even for migraines, clotting risk)

• 3 options:
  • **Copper IUD** = most effective option: <0.1% pregnancy rate if inserted within 5 days
  • **Ulipristal acetate**, requires prescription, single dose of 30 mg, 0.9% to 2.1% pregnancy rate if taken within 72 hours
  • **Oral levonorgestrel**, available without prescription, single 1.5 mg dose, 0.6% to 3.1% pregnancy rate if taken within 72 hours
    • Women who weigh >165 lbs should use levonorgestrel only if they have a difficult time obtaining a ulipristal prescription or IUD placement; the pregnancy rate for women with a body mass index of ≥30 kg/m² who use levonorgestrel as EC is 5.8%, compared with 2.6% for those who take ulipristal
Conclusions

- Patients on teratogenic drugs need to be fully counseled about all contraception options
- Remember to register for REMS programs! (esp easy to overlook for mycophenolate)
- Don’t forget about emergency contraception
- Spironolactone is a great option for women with acne
- Advocate for our patients
  - Gender neutral classification
  - Reducing burden of iPledge for patients who cannot become pregnant and for women using highly effective LARC