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## The Use Of Low Dose Oral Contraceptives for the Management of Acne

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### ABSTRACT

*There is compelling evidence that oral contraceptives (OCs) are effective in the management of mild-moderate acne vulgaris, as well as cumulative evidence that elevated levels of androgens in acne patients, relative to appropriate controls, are an underlying pathophysiological factor in acne. All low dose OCs reduce serum free testosterone (T) to a similar extent, which is contrary to the traditional concept that a patient who has acne should not use an OC containing a progestin with androgenic properties. The efficacy of various OCs to improve acne has been reported in transverse, cohort and comparative studies, and more recently in multicenter, randomized, placebo-controlled trials. Recently, an ultra-low dose OC (Alesse<sup>®</sup>, Wyeth) was shown to effectively reduce non-inflammatory and inflammatory lesions in mild-to-moderate acne, while having a profile of side-effects similar to that of a placebo. Besides its contraceptive efficacy, an ultra-low dose OC represents an attractive alternative as a single or associated medication in the management of acne.*

**Key words:** acne, androgens, anti-androgens, antibiotics, oral contraceptives

An ultra-low dose oral contraceptive (Alesse<sup>®</sup>, Wyeth) containing 20µg ethinyl estradiol (EE) and 100mg levonorgestrel (LNG) was approved by TPP Canada for the treatment of mild-to-moderate acne in January 2002.<sup>1,2</sup> Its contraceptive efficacy has been corroborated by ultrasonic evaluation of the ovaries showing inhibition of follicular development, and by hormonal measurements demonstrating suppression of estradiol and progesterone.<sup>3</sup> It provides menstrual cycle control and tolerability that is equivalent to that of OCs containing 35µg of EE.<sup>4</sup>

### Excess Androgens in Acne

A common notion is that neither acne vulgaris nor idiopathic hirsutism is associated with high serum levels of androgens in the absence of other associated signs and symptoms of hyperandrogenism. The range of reference androgen values has been established in laboratories mainly to rule out a secreting tumor. There is no established stratification of normal ranges to estimate androgen values for benign androgen conditions such as acne, hirsutism and polycystic ovarian syndrome. In this context, many believe that serum androgens are not elevated in typical acne. However, when appropriate controls were used, androgens of adrenal or ovarian origin increased in women presenting with otherwise unexplained acne<sup>5-10</sup> A recent study demonstrated that serum T levels in acne patients were at least twice the level

of normal controls without acne.<sup>9</sup> Dehydroepiandrosterone sulphate (DHEAS) was also found to be elevated in acne patients when compared to a control group.<sup>9</sup> Recent data also showed no change in androgen metabolism (5 $\alpha$ -reductase and 17 $\beta$ -hydroxysteroid dehydrogenase) in sebaceous glands between subjects with and without acne, providing evidence against possible local production of androgens in this condition.<sup>8</sup> Thus, a relative increase in circulating ovarian and adrenal androgens appear to play a role in the pathophysiology of acne. The sebaceous gland, which is sensitive to androgens, and which is responsible for the associated seborrhea should be considered as an underlying pathophysiological component.

### Anti-Androgenic Action of Oral Contraceptives

Traditionally, clinicians believed that a patient with acne should not use an OC containing a progestin with androgenic properties.<sup>11</sup> Investigators have speculated that the androgenic effects of progestins evaluated in animal and *in vitro* systems may increase the likelihood of androgen-related side-effects, including acne and hirsutism. The evidence is to the contrary. The suppression of LH and FSH by OCs results in a decreased secretion of androstenedione and testosterone by theca cells in the ovary. Estrogen-progestin combinations also increase the level of sex hormone-binding globulin (SHBG), resulting in greater T binding and a reduction in free T. The use of an OC also causes a reduction in serum levels of ovarian and adrenal androstenedione, and of DHEAS, which originates exclusively from the adrenal glands. Thus, the use of an OC has complementary actions mainly to lower free T and the androgen precursors secreted by the ovaries and the adrenals. The decrease in androgen action is reflected by a diminution in 3  $\alpha$ -androstenediol-glucuronide, which is the cellular catabolite of DHT by the sebaceous gland among peripheral tissues sensitive to androgens.

Estrogen-progestin combinations differ somewhat in their efficacy to inhibit T production and to increase SHBG

levels. However, the net effect is similar for free T, which decreases by 40-50% in the average woman. Direct comparisons between various OC formulations show that they all reduce free T to the same extent.<sup>12,13</sup> Since free T is the ultimate effector of circulating androgens, all OCs have a similar potential for improving acne.

### Clinical Trials

Several studies have recognized a lower incidence of acne while using different OCs.<sup>14-17</sup> Five pilot studies have also reported a 50-80% improvement in comedone counts, as well as in the numbers of papules and pustules after a few cycles of OCs containing various doses of EE and various types of progestins.<sup>13,18-21</sup> These observations have now been recently confirmed by four multicenter, randomized, placebo-controlled trials using a triphasic OC formulation containing 35 $\mu$ g EE and 180-215-250 $\mu$ g NGM (Tri-Cyclen<sup>®</sup>)<sup>22,23</sup> and the low dose monophasic combination of 20 $\mu$ g EE and 100 $\mu$ g LNG (Alesse<sup>®</sup>).<sup>24,25</sup>

Two similar Phase III trials (see Table 1) were conducted involving 35 $\mu$ g EE/180-215-250 $\mu$ g NGM (Ortho Tri-Cyclen<sup>®</sup>) vs. placebo for 6 months of treatment.<sup>22,23</sup> In the first study, 257 patients, aged 15 to 49 were randomized into a multi-center, double-blind, placebo-controlled trial if they had moderate acne (6-100 comedones, 10-50 inflammatory lesions, and fewer than 5 nodules). One hundred sixty patients completed the 6-month study in the efficacy evaluable population. The OC group showed a statistically significant improvement over the placebo group for all primary efficacy measures. The second trial included 250 women and the treatment group performed significantly better than the placebo group for all primary efficacy measures.<sup>22</sup>

The second series of clinical studies of OCs in acne involved the use of the lower estrogen OC, Alesse<sup>®</sup>.<sup>24,26</sup> Two outpatient, multicenter, randomized, double blind, placebo-controlled trials following a similar protocol were conducted to determine the effects of 20 $\mu$ g EE and

Author	OC Studied	N	Number Inflammatory Lesions			Regression of Lesions			Subject's Self-Assessment of Improvement		
			OC	Placebo	P	OC	Placebo	P	OC	Placebo	P
Redmond, et al <sup>22</sup>	Ortho-Tricyclen <sup>®</sup>	250	56.4%	34.6%	0.01	46.4%	33.9%	0.001	82.0%	47.0%	0.001
Lucky, et al <sup>23</sup>	Ortho-Tricyclen <sup>®</sup>	257	62.0	38.6%	0.0001	53.0%	26.8%	0.0001	91.0%	70.0%	0.001
Thiboutot, et al <sup>24</sup>	Alesse <sup>®</sup>	350	46.8	32.6%	0.027	39.9%	23.4%	0.004	88.0%	73.0%	0.05
Leyden, et al <sup>25</sup>	Alesse <sup>®</sup>	371	41.5	27.9%	0.016	29.7%	9.1%	0.001	81.0%	72.0%	0.03

**Table 1:** Results of four Phase III Clinical Trials for OCs in the treatment of acne.

100µg LNG (Alesse®) on the treatment of moderate acne. In the first study, healthy women, at least 14 years of age, with regular menstrual cycles and moderate facial acne were randomly assigned to receive the active treatment or placebo for 6 cycles. Inflammatory, noninflammatory, and total lesion counts at cycle 6 with 20µg EE and 100µg LNG (Alesse®) were significantly lower when compared to placebo. Patients in the OC group also had significantly better clinician global and patient self-assessment scores than those in the placebo group at cycle 6. Similar results were documented in the second trial with significant decreases in the mean inflammatory and total lesion counts after 6 cycles in the OC group compared to the placebo group.<sup>25</sup> In a sub study, biochemical markers of androgenicity were also assessed. Compared to placebo, use of this low dose OC resulted in significant reductions in free and bioavailable testosterone, androstenedione, 3α-androstanediol glucuronide (3α-G), and increased levels of SHBG after 6 cycles.

### Efficacy and Safety of Alesse® in Acne

One very interesting aspect of these studies was the unique opportunity to compare the side-effects associated with an OC to those of a placebo. In the 20µg EE and 100µg LNG (Alesse®) acne studies, symptoms usually attributed to the estrogen and/or progestin components of an OC were not different from those observed during the use of the placebo. As seen in Table 2, the very low dose EE/LNG combination did not induce significant modifications in the incidence of weight gain, breast tenderness, nausea, vomiting, headache and migraine.<sup>26</sup>

### OCs and anti-androgen agents

The estrogen-progestin combination Diane-35®, containing 35µg EE combined with 2mg cyproterone acetate, a progestin having direct anti-androgen effects, is known to be quite effective in the treatment of acne and hirsutism, although there is no Class I evidence (randomized, double-blind, controlled studies) supporting the efficacy of this prediction.<sup>27</sup> Several OC formulations have been compared

Adverse event	20µg EE and 100µg LNG (Alesse®) % (n=349)	Placebo % (n=355)	P-value *
Headache	31.5	30.1	0.74
Migraine	3.2	2.3	0.49
Nausea	14.0	11.3	0.31
Vomiting	2.6	1.7	0.44
Weight gain	3.4	2.3	0.37
Breast pain	4.6	3.1	0.33

**Table 2:** Alesse® vs. Placebo: frequency of adverse events commonly associated with OCs.

\* Fisher's exact.

Pooled data of intended to treat population.<sup>26</sup>

Placebo effects are commonly seen in dermatology trials, acne trials in particular. This can be explained in part by trial protocols that include careful skin-care (e.g., proper skin cleansing and avoidance of comedogenic skin-care products). Patient compliance with meticulous skin-care practices is encouraged by regular visits to trial investigators. Such skin care alone may have a positive effect on acne. Furthermore, acne is known to have a fluctuating course with regression to the mean over time in a given cohort of patients. Because of this, the trial period includes spontaneous improvement in some women and the resolution of some acne flares present at baseline. Finally, many dermatologists attribute the large placebo effect to investigator and patient optimism.

to Diane-35® and found to be as effective or somewhat less effective than this anti-androgenic combination.<sup>28-33</sup> However, comparisons were limited to 6 cycles of treatment and the side-effect profiles were not compared. Although there seems to be improvement of acne after treatment with the anti-androgen spironolactone (Aldactone®), the few studies done to date have been methodologically weak. There are, as yet, no reports for the treatment of acne using flutamide (Euflex®), a non-steroidal androgen receptor antagonist, or finasteride (Proscar®, Propecia®), an inhibitor of the 5-α-reductase enzyme converting T into the more active compound dihydrotestosterone (DHT) within the sebaceous gland. In theory, the addition of an anti-androgen would be more

effective in hirsutism than in acne, since excess androgens are the main causative factor in hirsutism, whereas other factors are involved in the pathophysiology of acne. In practice, prescribing an anti-androgen for women of reproductive age requires effective contraception to prevent the possible occurrence of fetal anomalies induced by a compound having direct anti-androgenic actions.

### Concomitant Use of OC and Antibiotics in Acne

Several pharmacokinetic and pharmacodynamic studies indicate that the antibiotics currently prescribed for acne treatment do not modify serum concentrations of EE and of various progestins.<sup>34-38</sup> They do not interfere with the suppression of gonadotropins (LH and FSH) and ovarian sex steroid hormones (estradiol and progesterone).<sup>35,36,39-41</sup> According to a recent bulletin from the American College of Obstetrics and Gynecology, the anti-infective agents tetracycline, doxycycline, ampicillin, metronidazole and quinolones do not reduce steroid levels in OC users.<sup>42</sup> In a recent review of available data, the Pearl Index (number of pregnancies per 1000 women years) during the concomitant use of antibiotics and various OCs in acne was established at 1.6, which favorably compares with the failure rate of users who have not taken antibiotics.<sup>43</sup> However, these data have been estimated on rather small numbers. In one Australian study, 209 inadvertent pregnancies in oral contraceptive users were studied to determine the associated factors. Forty-eight of the 209 patients (23%) took an antibiotic in the last two cycles before conception and were included as one of several reasons for OC failure.<sup>44</sup> Caution should be exerted and another effective contraceptive method should be used whenever a patient is taking other antibiotics or doses of antibiotics higher than those prescribed in the usual treatment of acne. The patient taking an antibiotic should also be told to use another effective contraceptive means in case she experiences diarrhea or breakthrough bleeding, which could then suggest decreased absorption or efficacy of the OC, or inadequate compliance.

### Conclusion

Based on the multiple factors involved in the pathogenesis of acne and on the severity of lesions, choosing one of the various treatment approaches depends on the needs of the patient and on the objectives of the physician. Dermatologists most frequently prescribe agents to normalize dyskeratinization and to reduce the proliferation of *P. acnes* and inflammatory skin changes. Sebum production, which is sensitive to a mild elevation of androgens can be reduced by a low dose OC. Besides its contraceptive and other non-contraceptive benefits, a low

dose OC has a side-effect profile similar to that of a placebo and has been determined to have significant efficacy in the treatment of mild-to-moderate acne. The effects of using an oral contraceptive are usually not seen in chemical practice for 3-6 cycles. The application of another acne treatment during treatment with an OC is actually done in regular practice, but has yet to be evaluated in clinical research studies.

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## Limited Breast Reduction by Liposuction

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### ABSTRACT

Traditionally, dermatologic surgeons have referred women seeking breast reduction to plastic surgeons for excisional mammoplasty. However, with recent advances in small cannula tumescent liposuction surgery, referral for such surgery may be unnecessary in some cases. Breast liposuction can reduce the size of female breasts that have essentially normal architecture with a minimum of visible scarring and an aesthetically pleasing result. We describe a method for liposuction reduction of female breasts that is safe, efficacious, and associated with high levels of patient satisfaction. Liposuction for breast reduction in women is an appropriate addition to the array of liposuction procedures available to the dermatologic surgeon.

**Key Words:** liposuction, breast reduction

### *A Brief History of Liposuction*

Liposuction is the aesthetic removal of undesirable localized collections of subcutaneous adipose tissue. The procedure was developed in the mid-1970's by Georgio and Arpard Fischer and advanced with innovative suctioning equipment created by Yves-Gerard Illouz. The technique of tumescent anesthesia introduced by Jeffrey Klein in 1987, significantly improved safety while reducing the complications associated with the procedure. Refinement of liposuction methods has enabled physicians to treat challenging areas such as arms, inner thighs, neck and jowls and more recently the female breast.

### *Breast Reduction Strategies*

Breast reduction by liposuction includes several approaches. Traditional breast reduction surgery may be preceded or followed by moderate volume liposuction. Adjunctive use of liposuction can be useful for thinning pedicles, removing axillary and lateral chest wall fat, contouring the inframammary fold, and adjusting volume to correct asymmetries after conventional bilateral reduction mammoplasty. Alternatively, modest breast hypertrophies can be initially treated by liposuction, with the extent of further excisional mammoplasty dictated by the quantity of residual tissue. This approach is also used to treat congenital asymmetry in adolescents and to correct pseudoptosis. During the last decade, liposuction alone has been used for reducing mild gynecomastia that entails excess breast fatty tissue but near-normal glandular breast tissue. In 1991, Alan Matarasso and Eugene Courtiss<sup>1,2</sup> reported that liposuction alone could reduce

each treated breast by 75-475cc in patients aged 18 to 60. One to five-year follow-up found no fat reaccumulation or breast reenlargement.

### *Advantages of Breast Reduction by Liposuction*

Breast liposuction can give dramatic results and offer significant advantages over surgical reduction. Unlike traditional approaches, breast liposuction does not require glandular resection and movement of the nipple-areola complex on a local pedicle. Thus, the inverted T-shaped scar is avoided, and scars after lipectomy are virtually undetectable if the inframammary/axillary line approach is used. Since there is no cutting of breast tissue, more vessels, nerves, parenchyma and supporting connective tissue are left intact so there is minimal disturbance to sensation and lactation. From the standpoint of the surgeon, no pedicle, flap or dissection is required, and no parenchymal structures are transected. There is a consequent dramatic decrease in reported complications with liposuction alone compared to excisional breast reduction, which can in as many as 50-60% of patients induce infection, bleeding, hematoma, seroma, wound dehiscence, skin necrosis, hypertrophic scars or keloids, poor breast shape, loss or alteration of sensation, or inability to breast-feed. Since liposuction is a minimally invasive outpatient procedure performed under local anesthesia, postoperative wound care is minimal and recovery time is brief. Maintenance of the architecture of the breast, including neurologic, vascular, and glandular structures, results in preservation of sensation and symmetry.

### *Is Breast Liposuction Safe?*

Critics of liposuction for breast reduction have raised the possibility of interference with mammography.<sup>3</sup> Potential problems after liposuction have been proposed to include septal distortion from scarring, increased breast density due to selective extraction of fat, and extensive fat necrosis culminating in microcalcification. While post-liposuction mammograms demonstrate greater tissue density and an increase of parenchymal microcalcification, these post-liposuction calcifications are easily and reliably distinguished from malignant calcifications, which are less scattered, less regular, and more numerous.<sup>3,4</sup> To further protect the patient, before liposuction, a preoperative mammogram should be obtained. Within six months postoperatively, a repeat study should be done to detect changes due to liposuction alone.

### *Who Should Get Breast Liposuction?*

Certain criteria must be met for successful breast liposuction:<sup>1,2</sup>

- (1) The patient's skin tone must be sufficiently elastic for shrinkage to the post-operative contour. Patients with so-called "soft (non-elastic) skin" should be advised that they may be less than ideal candidates for breast reduction with liposuction alone.
- (2) The nipple-areola complex must be well-located and the relationship of the nipple to the inframammary crease satisfactory. Satisfactory nipple position is an anterior orientation that is not inferiorly deviated or ptotic. Liposuction alone cannot correct nipple ptosis, reduce the size of the nipple-areola complex, or relocate the complex. Women with mild breast ptosis may experience mild to moderate post-operative improvement in ptosis. However, the definitive treatment for ptosis remains cold steel breast reduction surgery.
- (3) The density of the breast must be appropriate. Treatable breast enlargement must be largely due to fatty tissue rather than excess glandular parenchyma, which is less amenable to liposuction.

Breast liposuction can provide a diminution of breast size of one to two cup sizes. Patients desirous of greater reduction should be counseled to consider excisional mammoplasty. Before breast liposuction, patients should receive a baseline mammogram. Anticoagulants and antiplatelet agents, such as vitamin E supplements and daily aspirin, should be discontinued a week in advance of

the procedure in consultation with the patient's primary care physician.

### *How is Breast Liposuction Performed?*

Preoperative measurement of breast weight utilizing a digital scale and volumetric measurement using water displacement can help the surgeon decide how much fat to remove and how the total should be distributed between the two breasts to ensure an even result. Multiple, usually two, stab incisions are made in the inframammary crease of each breast with a third incision placed in the anterior axillary line. Tumescent anesthesia is then infused per customary technique.<sup>5-6</sup> Infusion is performed throughout the entire breast as well as parallel to the plane of the chest wall. Approximately 600-800cc of tumescent solution is typically required to fill each breast and ensure that the deep portion of the breast adjacent to the chest wall is completely infiltrated. Thirty to forty-five minutes after tumescent infusion is complete, liposuction is initiated with appropriate cannulas, such as the 12-gauge Klein and 12-gauge Capistrano cannulas. Machine suction is performed via standard criss-cross triangulating technique, with fanning from each of the entry sites. Like tumescent fluid infusion, suction is best performed throughout the entire volume of the breast. It is essential that the surgeon continuously palpate and monitor breast size and symmetry during breast liposuction. The non-dominant hand is used to pinch and assess breast volume and contour as liposuction progresses. Superficial suctioning should be avoided, as should aggressive suctioning under the nipple complex. This process of conservatism and continual reevaluation increases the likelihood that breast symmetry and contour is maintained postoperatively. Additionally, many women benefit significantly from thorough, even fat removal from the lower outer quadrant of the breast. Treatment of this area can aid in volume reduction as well as skin retraction and mild breast elevation.

### *Results and Aftercare*

Suction volumes vary, with 250-500cc of fat typically removed from each breast. At the conclusion of suctioning, the surgeon can readily confirm breast size and symmetry by palpating the breast to estimate the residual volume, as well as by comparing volumes of fat removed from each breast during the procedure. Use of a compression binder or support bra after surgery is essential. Continuous use of such a device for the first three months after surgery ensures maximum smoothness and uniformity of the final contour. The initial postoperative compression garment is worn 23 hours/day

for the first 7 days, followed by the use of a properly fitted support bra 16-24 hours a day for the next 3 months. More so than with liposuction of other anatomic areas, the cosmetic end result is highly dependent on patient adherence to a strict regimen of garment use, and patients should be apprised of their vital role in this process.

## Conclusions

Liposuction for breast reduction in women is an appropriate addition to the array of liposuction procedures available to the dermatologic surgeon. Minimally invasive and sparing of the breast parenchyma, breast liposuction has an excellent safety profile and rapid recovery time. Cosmetically elegant, it provides symmetrical results with barely visible scarring. Minor reductions in breast size in patients with normal shaped breasts will look better after liposuction alone than any other type of breast reduction surgery. Patients requiring change in the overall shape or orientation of the breasts and nipples, elderly patients, and patients requiring high-

volume breast reduction should be referred to our plastic surgery colleagues for excisional procedures.<sup>7</sup>

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## INDUSTRY NEWS

### FDA Strengthens Controls and Issues Consumer Alert on Importing Certain Prescription Drugs

As part of its ongoing efforts to reduce preventable adverse events from the products it regulates, the US Food and Drug Administration (US FDA) announced in December 2002, that it is strengthening the controls designed to protect patients by restricting imports of certain prescription drugs that can be used safely only with specified controls in place.

The FDA's action involves adding these drugs to an existing FDA Import Alert, which alerts FDA field personnel to the possible importation of these drugs, provides guidance as to their detention and refusal of admission into the United States. It also advises US Customs personnel to refer any attempted importation to the local FDA field office.

The drugs added to the Import Alert are as follows:

- Accutane<sup>®</sup> (isotretinoin) - indicated for the treatment of severe recalcitrant nodular acne
- Actiq<sup>®</sup> (fentanyl citrate) - indicated for the management of severe cancer pain in patients who are tolerant to opioid therapy
- Clozaril<sup>®</sup> (clozapine) - indicated for the management of severe schizophrenia in patients who fail to respond to standard drug treatments for schizophrenia
- Lotronex<sup>®</sup> (alosetron hydrochloride) - indicated for the treatment of severe irritable bowel syndrome in women
- Mifeprex<sup>®</sup> (mifepristone or RU-486) - indicated for the medical termination of early intrauterine pregnancy
- Thalomid<sup>®</sup> (thalidomide) - indicated for the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum
- Tikosyn<sup>®</sup> (dofetilide) - indicated for the maintenance of normal sinus rhythm in patients with certain cardiac arrhythmias
- Tracleer<sup>®</sup> (bosentan) - indicated for the treatment of severe pulmonary arterial hypertension
- Trovan<sup>®</sup> (trovafloxacin mesylate or alatrofloxacin mesylate injection) - an antibiotic administered in in-patient health care settings for the treatment of severe, life-threatening infections
- Xyrem<sup>®</sup> (sodium oxybate) - indicated for the treatment of cataplexy in patients with narcolepsy

In a related action, the US FDA today alerted consumers not to buy these drugs over the internet, because drugs obtained via websites usually are not accompanied by these safety controls. The FDA is concerned about the safety risks posed by use of any of these products without the specified controls in place.

The revised Import Alert and the Consumer Advisory are available online at [http://www.fda.gov/ora/fiars/ora\\_import\\_ia6641.html](http://www.fda.gov/ora/fiars/ora_import_ia6641.html) and <http://www.fda.gov/oc/buyonline/consumeralert120902.html> respectively.

Although these drugs have important benefits for many patients, they have serious known risks and so are available in the US only under specially created safety controls. These safety controls are bypassed when these drugs are purchased from foreign sources, placing patients who use these imported drugs at higher risk. Therefore, because of this higher risk to patients, the FDA took action to further curtail the products' availability from foreign sources. The drugs purchased from foreign sources are generally not FDA-approved.

Controls on these prescription drugs include limiting their distribution to specific facilities (such as hospitals); limiting their distribution to physicians with special training or expertise; or requiring certain medical procedures (such as pregnancy testing or blood testing) with their use.

Detailed information for consumers and patients who would like to learn more about how to buy prescription drugs safely may be found in FDA's guide, "Buying prescription Medicines Online: A Consumer Safety Guide," available online at <http://www.fda.gov/cder/drug/consumer/buyonline/guide.htm>.

Source: US FDA News Release

#### PATIENT ALERT

## American Academy of Dermatology Stresses the Safe Use of Botulinum Toxin

Since the Food and Drug Administration (FDA) approval of one form of botulinum toxin, it has been widely reported that patients are attending so called "Botox<sup>®</sup> parties" for the administration of this drug. Botulinum toxin treatments being performed in casual social settings rather than in a controlled medical environment contradicts the seriousness of this medical procedure.

As with any medical procedure, the possibility of adverse effects occurring from a botulinum toxin injection is always a possibility. Adding alcohol to the mix is a bad idea for a number of reasons, especially since bruising can be intensified.

Botulinum toxin is a purified form of one of the most potent toxins in the world. In high doses, it can cause the clinical disease botulism. However, when carefully injected by dermatologists and dermatologic surgeons in very low doses, botulinum toxin is a modern tool that can reduce the signs of aging. The American Academy of Dermatology (AAD) urges patients to select a qualified physician, such as a dermatologist, when considering this or any cosmetic procedure.

Because this is a quick method to treat wrinkles with no downtime, many patients are compromising their safety by having this medical procedure performed in an inappropriate setting, often by untrained medical professionals. To assist patients in choosing a qualified physician, the AAD recommends that before undergoing any cosmetic procedure, patients should ask the following questions:

- What are the doctor's credentials? Is he/she a board-certified dermatologist or other appropriately trained surgeon? Ask to see their credentials.
- How many of these cosmetic surgery procedures has the physician performed?
- What results can be expected?
- How long is the recuperation period? Ask to see before and after photos of the physician's previous patients.
- What are the risks?
- Where is the cosmetic surgery usually performed?
- What is the cost?

The AAD encourages all patients to consult with their dermatologist to determine which treatment is best for them. A well-informed patient and a skilled dermatologist are always the best prescription for a successful outcome.

For more information, contact the AAD at 1-888-462-DERM (3376) or [www.aad.org](http://www.aad.org).

Source: AAD News Release

## Update on Drugs

Class	Name/Company	Approval Dates and Comments
<i>Autoimmune Disease</i>	<b>Prasterone</b> <i>Prestara</i> <sup>™</sup> Genelabs Technologies	The US FDA issued an approvable letter in August 2002, for treating women with systemic lupus erythematosus (SLE). A Genelabs study demonstrated a positive effect on bone mineral density in women with mild-to-moderate SLE who were taking low doses glucocorticoids. Approval is contingent on the successful completion of an additional clinical trial confirming this positive effect.
<i>Antiviral Agent</i>	<b>Valacyclovir HCl</b> <i>Valtrex</i> <sup>®</sup> GlaxoSmithKline	The US FDA approved a supplemental new drug application in September 2002, for the treatment of cold sores in healthy adults. It is the first one-day, oral antiviral medication shown to shorten the duration of a cold sore outbreak.
<i>Hormonal Preparations</i>	<b>Norelgestromin/Ethinyl Estradiol Transdermal System</b> <i>EVRA</i> <sup>®</sup> Janssen-Ortho	TPP Canada approved this transdermal product in August 2002, for birth control. This contraceptive patch is applied once/week and the first one to be approved by Health Canada.
Drug News		
<i>Drug Warning</i>	Pharmacia has issued a "Dear Health Care Professional" letter recommending that valdecoxib (Bextra <sup>®</sup> ) not be given to any patient with a previous allergic reaction to sulfonamides, and that it should be stopped at the first sign of a skin rash or hypersensitivity reaction. This nonsteroidal anti-inflammatory agent (NSAID) was recently linked to a risk of hypersensitivity reactions (i.e., anaphylaxis, angioedema) and potentially severe skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, and erythema multiforme. Furthermore, some of the more life-threatening reactions occurred in patients with a history of allergic reactions to sulfonamides.	
<i>Oncologic Agent</i>	Allergan has entered into a research collaboration and license agreement for the right to develop and commercialize PEP005, a topical treatment for non-melanoma skin cancer and actinic keratosis from Peplin Biotech, a biomedical research company based in Brisbane, Australia. This product has shown early promise in pre-clinical studies and in a small open-label human proof of principle clinical study for the treatment of a wide range of human cancers, including melanoma and other skin cancers. Allergan will have exclusive license to develop and market this product for the topical and intralesional treatment of skin and eye conditions in North and South America.	
<i>Drug Warning</i>	The Institute for Safe Medication Practices recently reported cases of accidental daily administration of oral methotrexate where weekly dosing was intended. Some cases have resulted in fatalities. They state that because of the number of fatalities from errors, clinicians should consider it a high alert medication.	

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Articles are indexed by drug names, trade-names, and disease terms.

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