

## Dermatologic Drugs Advisory Committee, FDA 1988

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Dr. Del Vecchio -- Hoffmann-LaRoche

(pg 110) "...you see an interesting trend here from 1983 to 1987. The number of new female patients has dropped from 141,000 to 80,000...In 1987, approximately one-half the number of women of child-bearing age were treated with Accutane as were treated in 1983 in terms of new patients."

"I would submit to you that far from increased and indiscriminate use, that these data show that in fact prescriptions have decreased sharply since the first reports of congenital malformations in 1983, and the information that went out in 1983 and 1984. I think this is a very clear indication of two possible reasons here."

"One is the congenital malformations, and the increased care with which dermatologists and other physicians are prescribing this drug in this age group; and second, perhaps this says something about the efficacy of Accutane and that we may be approaching whatever that baseline incidence is."

"Just to put this figure into perspective, just as Dr. Strauss put the figure into perspective before, that is Dr. Graham's figures were correct, that the average dermatologist would see less than one patient per year who is a woman in this age group who requires Accutane. To put that figure in perspective, it would mean that the average dermatologist would see one new female patient per month who requires Accutane therapy."

"I would ask those of you who are dermatologists on the Advisory Committee and in the audience if that does not in fact reflect what would seem to be a reasonable approach to the use of this particular product, and that it is not any more rare than that."

"I am not standing here claiming that every one of those 61,000 patients met the exact criteria for severe recalcitrant cystic acne..."

(pg 112) "Again, I am not saying that 98.5 percent of all Accutane prescriptions are directly related to the package insert diagnosis, but we are certainly not dealing with 93 percent in the other direction..."

(pg 113) "...If our figures are nearly correct, we are talking about one new female patient who requires Accutane per dermatologist per month..."

Dr. Bergfeld -- chair of Committee(pg 272)

"It appears to me that the Committee, by consensus, feels that there should be restriction of this drug by some method. I would like to go over the things that were mentioned during the comment period to state some of the restrictions that you have actually put on this. We have dealt with four different areas, restriction of the actual distribution of the drug, restriction of two special physicians for distributing the drug, restriction of special patients who get the drug, and the necessity of having a second opinion in those high risk females."

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Dr. Spraker -- member of the Committee(pg 20)

"The suggestion that Accutane usage be decreased by 20 percent is both arbitrary and impractical."

Dr. Richard Miller -- Teratology Society (pg 31)

"The manufacturer has estimated that women aged 12 to 44 have received 65,000 new Accutane prescriptions during 1988. The number of prescriptions seem to be well above the published estimates of the incidents for recalcitrant cystic acne."

Dr. Evans -- FDA staff (pg 41)

"The goals of these activities are to reduce the prescribing of Accutane..."

Dr. Wm Cunningham -- Hoffmann-LaRoche (pg 45)

"I will outline some of the epidemiology of the usage of the drug. In this regard, I would say that we share Dr. Evans' concern about the usage. We've seen a steady downward trend in the usage of the drug over the years, and I'll give you more specifics on that later. There's a clear reduction, as well in the number of

malformations over the years, and we find that a very positive sign that the events of 1983 and '84 and the events of 1988 have had an impact where it counts, that is, in reducing human malformations....

(pg 49)... We don't have true figures on the incidence of nodular cystic acne. The National Health and Nutritional Examination's Survey data is often quoted. I feel that this data is not reliable for the purpose in which it is being used because there were no established criteria for making the diagnosis of nodular cystic acne...

...my calculations indicate that between 30,000 and 75,000 female patients might require Accutane therapy per year in the United States...

(pg 50) In preparing for this presentation, I have asked other recognized experts in the field of acne, as well as a few practicing dermatologists to estimate the number of women of childbearing age who they think the average dermatologist might elect to treat with Accutane each month. The figures that they estimated ran up to one half to one patient per month and considering the fact that there are approximately 7,000 practicing dermatologist in the United States, my calculations reveal that between 40,000 and 84,000 women of childbearing potential might be candidates for Accutane each month.

If one compares these figures to the actual usage of the drug, the numbers are in a similar range... Although with the new pregnancy warning program, it's my belief that the number of patients who are going to be treated will be decreased.

(pg 70) I'd like to very briefly demonstrate some of the usage that illustrates the downward trend in total patients, new patients, and most importantly in new female patients. I think you can see from this graphic display that the usage of the drug peaked in 1983.

(pg 71)...but between 1987 and 1988, there was a more significant downward trend in the usage of the drug in new female patients.

...It is very difficult to convert those factory units into actual patient numbers because of difference in dosage and duration of therapy, but we do see a downward trend. Furthermore, in early 1989, we also see a downward trend in the usage of the drug in terms of factory units.

(pg 86)The advertising you've seen is rather dramatically focused on contraindication and proper usage of pregnancy prevention. It is not focused on usage. The two ads you've seen are representative of the type of advertising you will see in the future.

(pg 87)...and the downward trend in usage, we feel is also a sign that the physician and the patient is truly aware that the goals of using this in severe recalcitrant cystic acne and excluding pregnancy and ensuring contraception are meaningful to them.

(pg 89)...We've been very careful not to promote the drug to non-dermatologists..."

Dr. Stadel -- FDA staff (pg 95)

"...One estimate, using the data from the N Haines, National Health and Nutrition Examination Survey is an incidence of about 5,000 new cases per year applying the definition that was used in relation to the IND."

Dr. Woodley -- member of the Committee (pg 105)

"...Dr. Strauss who's an acknowledged national, international expert in acne and who basically stated that he feels that the indication for acne is about right. That 3 percent of woman with acne actually have nodular cystic form that is recalcitrant."

Dr. Cunningham -- Hoffmann-LaRoche (pg 107)

"...new females for 1988 of the 65 to 70,000 new females for 1988, I think that the concern has been raised repeatedly that the usage at that level is too high for many of you on the committee and many of you in the audience. What I've tried to say today is that the usage trends we believe are down to some extent and that we see some usage trends in 1989 in our own factory units that tend to go downward as well."

Dr. John Strauss (pg 110)

"First of all, there are no good surveys that show you the true incidence of either nodular cystic acne..."

What I said was that I thought that there was probably between 2 and 5 percent of the women who had acne who probably warrant treatment with this. I also said that there probably were somewhere

between one-half and one patient per month that the average practicing dermatologist might need to put on Accutane."

Dr. R. Roberts -- AAP (pg118)

"...conclusion is that the drug is being excessively and inappropriately prescribed."

### **Dermatologic Drugs Advisory Committee, FDA 1990**

Dr. Nelson -- FDA staff (pg 99)

"I want to close my briefing by reviewing FDA's current concerns. They are the continued high level of Accutane use in the population at risk; prescriber noncompliance with vital components of the program, both of which increase the probability for pregnancy exposure and its range of adverse outcomes. In addition, we are concerned with relatively low enrollment in the impact assessment survey and that fact leaves us with the inability to rigorously assess the occurrence of pregnancy exposures and the inability to rigorously assess congenital defects."

Dr. Dan -- Hoffmann-LaRoche (pg 102)

"...Based on PDS data, it was estimated that approximately 130,000 women of childbearing age were exposed to Accutane therapy in 1988 and 1989 combined..."

Dr. Armstrong -- Hoffmann-LaRoche (110)

"So our conclusions are that utilization of Accutane by women of childbearing age decreased in 1988 and decreased dramatically more in 1989."

Dr. Mitchell --- Slone Epi Unit, BU (pg121)

"...we are likely to have approximately 40,000 enrollments a year...it is important to stress that our current enrollment rate is 53 percent..."

(pg 125) We also considered the number of women who reported having a pregnancy test before starting Accutane...This was apparently a disturbing finding, 40 percent of women interviewed reported having no pregnancy test."

Dr. Graham -- FDA (pg 147)

"The sponsor has applied a regression line from data in 1983 down through the data in 1989 and found a "statistically significant" downward slope. This observation is driven by the high number of prescriptions in 1983...the flattening of prescriptions for 2 consecutive years..."

(pg 159)...The number of women treated with Accutane, 65,000 in 1989...

(pg 172)...Our estimate of disease incidence is under 5000 per year. Yet, last year 65,000 women were newly started on the drug. This level is unchanged from 1989."

Dr Sid Wolfe -- (pg 182)

"...The United States rate of 252 16-38 year old women per year of marketing is 9 times higher than the rate in West Germany and 6.7 times higher than the rate in the United Kingdom."