

**Summary of Reported Cases of
Suicide and Depression in U.S.
Accutane-Treated Patients**

Diane K. Wysowski, Ph.D.

1

**Suicides Reported in U.S.
Accutane-Treated Patients from
Marketing (8/82) to May 2000**

Suicides DURING Accutane use	24
Suicides AFTER STOPPING Accutane use	13
Total	37

2

Reported Suicides: Patient Profile

Gender	84 % male
Median age	17 years
Median time on Accutane to suicide	~ 3 months
Median time after stopping Accutane to suicide	~2.5 months

3

Reported Suicides: Patient Profile

Psychiatric history	22 %
Other possible contributing factors*	57 %
Psychiatric history and/or other possible contributing factors	62 %
Reports received in 1998	49 %
Median peak dose	1 mg/kg/day

* E.g., relationship problems, stressful life events, substance abuse, family history

4

**Hospitalizations Reported for Depression,
Suicidal Ideation, and Suicide Attempts
from Marketing (Aug 82) to May 00**

Hospitalizations DURING Accutane use	85
Hospitalizations AFTER STOPPING Accutane use	25
Total	110

5

**Reported Hospitalizations for
Depression: Patient Profile**

Gender	56 % female
Median age	17 years
Median time on Accutane use to hospitalization	~1 month
Median time from stopping Accutane to hospitalization	3 months

6

Reported Hospitalizations for Depression: Patient Profile

Psychiatric history	44 %
Other possible contributing factors	52 %
Psychiatric history and/or other possible contributing factors	69 %
Reports received in 1998	41 %
Median peak dose	1.1 mg/kg/day

7

Reported Hospitalizations for Depression: Patient Profile

- Dechallenge:
 - 32 % had positive dechallenge with psychiatric treatment
 - for 29%, depression persisted in patients after Accutane was stopped
- Rechallenge:
 - 1 positive
 - 3 negative (with alcohol abstinence, dose lowering and continued use of an antidepressant)

8

Non-Hospitalized Depressions Reported from Marketing (Aug 82) to May 00

Non-hospitalized depression	284
-----------------------------	-----

9

Reported Non-Hospitalized Depressions: Patient Profile

- 45% of reports were received in 1998
 - following the February 98 labeling change, Dear Doctor letter, FDA Talk Paper, and media publicity
- 52% had accompanying physical symptoms
- 50% of reports were submitted by consumers and relatives

10

Top Ten Adverse Events for U.S. Accutane-Treated Patients in AERS

	No. of Reports
#1 Alopecia	1601
#2 Headache	1064
#3 Dry skin	1000
#4 Arthralgia	813
#5 Hyperlipidemia	768
#6 Depression	680
#7 Dermatitis	524
#8 Acne	505
#9 Condition aggravated	490
#10 Myalgia	472

11

**Degree of Underreporting is
Unknown and is Often
Substantial**

12

6

Supportive Evidence from Reports of a Possible Association Between Accutane and Depression

- Large number of serious reports
- Temporal association
- Positive dechallenges
 - most with psychiatric treatment
- Positive rechallenges

13

Supportive Evidence from Reports of a Possible Association Between Accutane and Depression

- Lack of psychiatric history and contributing factors in some individuals
- Similar case reports in literature

14

Complicating Factors

- Individuals with previous courses without depression
- High rates of depression and suicide in age group
- Presence of possible contributing factors -- acne itself, previous psychiatric history, other factors

15

Complicating Factors

- Symptoms often did not abate with drug discontinuation only

16

Inconclusive Evidence

- A large retrospective cohort study, funded by HLR, found no increased risk of depression in patients prescribed Accutane compared with those prescribed antibiotics for acne
- Study had serious limitations

17

Jick Study--Limitations

- Depression under-diagnosed
- Small sample size for studying suicide
- No data on acne severity
- No data on dose
- Questionable applicability of results to U.S.
- Limited U.S. data
- Data on suicides combined with suicide attempts

18

Conclusion

- The FDA has received reports of suicide and depression in U.S. Accutane-treated patients
- Case reports are suggestive of an association with Accutane, but do not allow definitive determination as to whether Accutane causes depression and suicide in treated patients

19