

Edgar Filing: JAZZ PHARMACEUTICALS INC - Form 425

JAZZ PHARMACEUTICALS INC

Form 425

December 08, 2011

Filing under Rule 425 under the Securities Act

of 1933 and deemed filed under Rule 14a-6 of

the Securities Exchange Act of 1934

Filing by: Jazz Pharmaceuticals, Inc.

Subject Company: Jazz Pharmaceuticals, Inc.

SEC File No. of Jazz Pharmaceuticals, Inc.:

001-33500

Registration No. 333-177528

The following is a slide presentation relating to the proposed transactions described therein that was made available beginning on December 7, 2011.

December 7, 2011  
Investor Relations

Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to Jazz Pharmaceuticals

growth  
potential  
and  
future

financial  
performance,  
including  
2011

financial  
guidance,  
and

statements related to the anticipated consummation of the business combination transaction between Jazz  
Pharmaceuticals

and

Azur

Pharma

Public

Limited

Company

(formerly

Azur

Pharma

Limited),

including

the

timing

and

benefits

thereof.

These

forward-looking

statements

are

based

on

Jazz

Pharmaceuticals

current

expectations

and

inherently

involve

significant

risks

and

uncertainties.

Jazz

Pharmaceuticals

actual

results

and

the timing of events could differ materially from those anticipated in such forward looking statements as a result of these risks and uncertainties, which include, without limitation, risks related to: Jazz Pharmaceuticals dependence

on  
sales  
of  
Xyrem  
®  
and  
Luvox  
CR  
®  
products  
and  
its  
ability  
to  
increase  
sales  
of  
its  
Xyrem;  
competition,  
including  
potential  
generic  
competition;  
Jazz  
Pharmaceuticals  
dependence  
on  
single  
source  
suppliers  
and  
manufacturers;  
the  
ability  
of  
Jazz  
Pharmaceuticals  
to  
protect  
its  
intellectual  
property  
and  
defend  
its  
patents;  
regulatory  
obligations  
and

oversight;

Jazz

Pharmaceuticals

cash

flow;

and

Jazz

Pharmaceuticals

ability to complete the transaction with Azur Pharma on the proposed terms and schedule and achieve the anticipated benefits of the transaction. These and those other applicable risks are described in more detail

under

the

caption

Risk

Factors

and

elsewhere

in

Jazz

Pharmaceuticals

Securities

and

Exchange

Commission

( SEC )

filings

and

reports,

including

in

its

Quarterly

Report

on

Form

10-Q

for

the

quarter

ended

September

30,

2011 and definitive proxy statement related to the Azur Pharma transaction. Jazz Pharmaceuticals undertakes

no

duty

or

obligation

to

update

any

forward-looking  
statements  
contained  
in  
this  
presentation  
as  
a  
result  
of  
new  
information, future events or changes in its expectations.

2  
"Safe  
Harbor"  
Statement  
under  
the  
Private  
Securities  
Litigation  
Reform  
Act  
of  
1995

3

**Additional Information**

**Additional Information and Where to Find It**

In connection with the proposed transaction between Jazz Pharmaceuticals and Azur Pharma, the companies have filed documents with the SEC, including the filing by Jazz Pharmaceuticals of a definitive proxy statement relating to the proposed and related matters, and the filing by Azur Pharma of a registration statement on Form S-4 that includes the definitive proxy statement/prospectus relating to the proposed transaction and related matters. The definitive proxy statement/prospectus has be



mailed to Jazz Pharmaceuticals stockholders in connection with the proposed transaction. INVESTORS AND SECURITY HOLDERS ARE URGED TO READ THE REGISTRATION STATEMENT ON FORM S-4 AND THE RELATED DEFINITIVE PROXY STATEMENT/PROSPECTUS BECAUSE THEY CONTAIN IMPORTANT INFORMATION ABOUT JAZZ PHARMACEUTICALS PHARMA, THE PROPOSED TRANSACTION AND RELATED MATTERS. Investors and security holders may obtain free documents and other related documents filed with the SEC at the SEC's web site at [www.sec.gov](http://www.sec.gov), or by directing a request to Jazz Pharmaceuticals Investor Relations department at Jazz Pharmaceuticals, Inc., Attention: Investor Relations, 3180 Porter Drive, California 94304, to Jazz Pharmaceuticals Investor Relations department at 650-496-2800 or by email to [investorinfo@jazzpharmaceuticals.com](mailto:investorinfo@jazzpharmaceuticals.com). Investors and security holders may obtain free copies of the documents filed with the SEC on Jazz Pharmaceuticals website at [www.jazzpharmaceuticals.com](http://www.jazzpharmaceuticals.com) under the heading Investors and then under the heading SEC Filings.

Jazz Pharmaceuticals and its directors and executive officers and Azur Pharma and its directors and executive officers are deemed participants in the solicitation of proxies from the stockholders of Jazz Pharmaceuticals in connection with the proposed transaction. Information regarding the special interests of these directors and executive officers in the proposed transaction is in the proxy statement/prospectus described above. Additional information regarding the directors and executive officers of Jazz Pharmaceuticals is also included in Jazz Pharmaceuticals proxy statement for its 2011 Annual Meeting of Stockholders, which was filed with the SEC on April 12, 2011. These documents are available free of charge at the SEC's web site and from Investor Relations at Jazz Pharmaceuticals as described above.

This communication does not constitute an offer to sell, or the solicitation of an offer to sell, or the solicitation of an offer to subscribe for or buy, any securities nor shall there be any sale, issuance or transfer of securities in any jurisdiction in which such solicitation or sale would be unlawful prior to registration or qualification under the securities laws of any such jurisdiction. For full prescribing information refer to product websites.

Building Shareholder Value by Focusing on Patient Needs  
Jazz Pharmaceuticals  
mission is to improve  
patients  
lives by identifying, developing and  
commercializing valuable pharmaceutical  
products in focused therapeutic areas



5  
Pursue lower risk  
development of  
specialty products  
Invest percentage  
of sales longer-term  
3

Strategy to Build Shareholder Value

Grow Xyrem sales in  
current indications

Increased focus on  
achieving full potential

Acquire additional  
marketed or close to  
approval products

Leverage our expertise  
and infrastructure

2

1

Maintain entrepreneurial, ownership culture at the company

4

Make disciplined resource allocation decisions

Current Business Overview

\$39  
\$54  
\$97  
\$230-235  
1  
2010  
2009

2008

2007

2011G

\$143

\$0

\$25

\$50

\$75

\$100

\$175

\$200

\$125

\$150

\$225

\$250

Xyrem -

Strong Sales Growth

7

1.

Based on guidance provided on November 1, 2011. The company is not updating the prior guidance and actual results may dif



Xyrem is a Standard of Care in Narcolepsy

Only FDA-approved product for both cataplexy and excessive daytime sleepiness in patients with narcolepsy

Marketed in U.S. since 2002

Marketed in major European countries by  
UCB and in Canada by Valeant

Currently marketed in U.S. by 110-person specialty sales force

Over 9,000 patients on therapy, usually in conjunction with stimulant therapy

Distributed  
under  
proprietary  
Xyrem  
Success  
Program  
®  
8

The Burden of Narcolepsy

Affects 1 in 2000 in US

1

multiple  
sclerosis

and  
Parkinson's  
disease  
2

> cystic fibrosis  
3

Although narcolepsy is thought to affect between  
125,000 and 200,000 Americans, only about  
50,000  
are  
diagnosed  
4

Key symptoms can be debilitating

Cataplexy occurs in 60%-100% of patients

100% experience excessive daytime sleepiness

1.  
National Institute of Neurological Disorders and Stroke. [http://www.ninds.nih.gov/disorders/narcolepsy/detail\\_narcolepsy.htm](http://www.ninds.nih.gov/disorders/narcolepsy/detail_narcolepsy.htm)
  2.  
Narcolepsy Sleep Foundation. [www.sleepfoundation.org/article/sleep-related-problems/narcolepsy-and-sleep](http://www.sleepfoundation.org/article/sleep-related-problems/narcolepsy-and-sleep). Accessed March 17, 2011.
  3.  
Zemanick et al. J Cyst Fibros. 2010;9:1-16.
  4.  
American Sleep Association. <http://www.sleepassociation.org/index.php?p=aboutnarcolepsy>. Accessed March 17, 2011.
- 9

-80  
-60  
-40  
-20  
0  
Placebo (n=33)  
XYREM 6 g/night (n=31)

XYREM 9 g/night (n=33)

-40

-30

-20

-10

0

Xyrem has Demonstrated Effect

on Two Key Symptoms of Narcolepsy

XYREM

6 g/night

(n=58)

XYREM

9 g/night

(n=47)

Placebo

(n=59)

16%

\*

37%

\*

3%

Improvement in Epworth

Sleepiness Scale

Week 2

Week 4

Baseline

Reduction in Weekly

Cataplexy Attacks

-28%

-49%\*

-69%+

10

1.

Trial

3:

From

a

8-week,

multicenter,

randomized,

double-blind,

placebo

controlled,

parallel-arm

trial

of

narcolepsy

patients

(N=228)

with

moderate  
to  
severe  
EDS  
and  
cataplexy  
symptoms.  
Antidepressants  
were  
withdrawn  
prior  
to  
randomization,  
and  
stimulants  
were  
continued  
throughout  
the  
study  
at  
stable  
doses.  
In  
XYREM  
clinical  
trials,  
80%  
of  
patients  
maintained  
concomitant  
stimulant  
use.  
XYREM  
International  
Study  
Group.  
J  
Clin  
2005;1:391.  
2.  
Trial  
1:  
From  
a  
4-week,  
double-blind,  
placebo-controlled  
trial

of  
narcolepsy  
patients  
(N=136)  
with  
moderate  
to  
severe  
cataplexy  
(median  
of  
21  
attacks  
per  
week)  
comparing  
the  
effects  
of  
three  
doses  
of  
orally  
administered  
sodium  
oxybate  
with  
placebo  
for  
the  
treatment  
of  
narcolepsy.  
Patients  
continued  
to  
receive  
stable  
stimulant  
therapy  
throughout  
the  
study.  
The  
US  
XYREM  
Multicenter  
Study  
Group.  
Sleep.



2002;25(1):42-29.

1

2

Sleep Med.



Most Common Adverse Events in  
Controlled Studies of Xyrem

Adverse Event

% of Patients (N=655)

Placebo

2

Xyrem

3

Nausea

4

19

Dizziness

4

18

Headache

15

18

Vomiting

1

8

Somnolence

4

6

Urinary

incontinence

4

<1

6

Nasopharyngitis

5

6

Label includes boxed warning that sodium oxybate is a central nervous system

depressant with abuse potential and should not be used with alcohol or other CNS depressants. See complete boxed warning at end of presentation.

11

1. Occurring in

5% of XYREM patients and more frequently than with placebo. 2. Data on file, Jazz Pharmaceuticals, Inc. 3. XYREM (sodium

1

Update on FDA Form 483 and Related Warning Letter

Fully committed to accurate and timely adverse event (AE) reporting

After receipt of FDA Form 483 in May, immediate actions initiated to improve AE reporting procedures:

Implemented additional procedures at central pharmacy

Strengthened AE collection and reporting systems, including revised SOPs

Improved training and auditing programs

Timely response to October FDA warning letter submitted

Ongoing oversight strengthened to ensure robust safety reporting systems

12

Strong Sodium Oxybate Patent Coverage

\* Listed in FDA Orange Book

13

Number

Issue Date

Expiration Date

Distribution system patent\*

7,765,106  
7/27/2010  
6/16/2024  
Distribution system patent\*  
7,765,107  
7/27/2010  
6/16/2024  
Distribution system patent  
7,797,171  
9/14/2010  
6/16/2024  
Distribution system patent\*  
7,668,730  
2/23/2010  
6/16/2024  
Distribution system patent\*  
7,895,059  
2/23/2011  
12/17/2022  
Formulation patent\*  
6,780,889  
8/24/1999  
7/4/2020  
Formulation patent\*  
7,262,219  
8/28/2007  
7/4/2020  
Process patent  
6,472,431  
10/29/1999  
12/22/2019  
Method of use patent\*  
7,851,506  
12/14/2010  
12/22/2019



## Overview of Manufacturing and Distribution

DEA drug quota needed to manufacture controlled Schedule I  
API

Exclusive relationships with API supplier and finished goods  
manufacturer:

Siegfried approved by FDA for API supply

Unique proprietary distribution system uses exclusive single pharmacy

Risk management program and unique product attributes require high touch capabilities

14

Current Xyrem Patient Coverage Distribution\*

Approximately 90% of insured patients  
have access

Relatively low rates of required prior  
authorizations

Low monthly out-of-pocket (OOP)  
expenses

Over 70% of patients have monthly  
OOP of  
\$50

\* Company data and MediMedia Formulary Compass: Sep/Oct 2011.

Medicare Part D

15

Commercial

8%

4%

1%

9%

Patient

Assistance

Program

Cash

Medicaid

78%

Xyrem Growth Initiatives

16

New narcolepsy physician targets

Xyrem Success Program education

Patient services

-

Nursing program

-

Xyrem Patient Connection

-

Patient assistance programs

Increased Marketing Investment

Improve Market Penetration Over Time

Current Patients >9,000

Approximately 18% of 50K Diagnosed Narcolepsy Patients

17

1. National Institute of Mental Health. <http://www.nimh.nih.gov/health/publications/the-numbers-count-mental-disorders-in-america>. 2003;160:1-23. 2. B, et al. Am J Psychiatry. 2001;158:1904-1910. 4. Grabill K et al..Assessment of obsessive-compulsive disorder: a review.J A

et al. Am J Health Syst Pharm. 2000;57:1972-1978.

Luvox CR

®

-

Important Treatment Option for OCD

Indicated for obsessive compulsive  
disorder (OCD)

OCD affects ~ 2.2 million Americans

1,2

Often underdiagnosed

3,4

Difficult to differentiate from comorbidities

5

Only 43% of adults newly diagnosed with OCD received adequate treatment in the

year

after

their

first

visit

for

OCD

6

Label includes boxed warning regarding suicidality and antidepressant drugs.

See complete boxed warning at end of presentation.



Luvox CR  
Continued Sales Growth  
\$30  
\$6  
\$31-33  
1  
2009

2008  
2011G  
18  
\$0  
\$5  
\$10  
\$15  
\$20  
\$25  
2010  
2  
\$18  
\$35  
\$40  
\$27

1.  
Based on guidance provided on November 1, 2011. The company is not updating the prior guidance and actual results may differ.

2.  
Includes \$2 million of revenue recorded as a result of a change in the timing of when Luvox CR revenue is recognized. The company

19

2011 Guidance Reflects High Operating Leverage

1.

Based on guidance provided on November 1, 2011. The company is not updating the prior guidance and actual results may differ.

2.

Includes Azur transaction related expenses of \$10-11 million.

2010-

A  
2011-  
G  
1  
Total Product Sales  
\$170M  
\$261  
268M  
Xyrem  
\$143M  
\$230 -  
235M  
Luvox CR  
\$27M  
\$31 -  
33M  
SG&A and R&D Combined

2  
\$95M  
\$114  
118M  
GAAP Net Income  
\$33M  
\$128  
131M  
Adjusted Net Income

3  
\$61M  
\$160  
163M  
GAAP EPS  
\$0.83  
\$2.76  
\$2.81  
Adjusted EPS

3  
\$1.55  
\$3.45  
\$3.50

Adjusted net income and adjusted EPS are non-GAAP financial measures that exclude certain items from GAAP net income and adjusted net income to GAAP net income and the related per share amounts is in a table included with this presentation.

3.

Strategic Transaction with  
Azur Pharma

21

Strategic Benefits

Diversified portfolio of CNS and  
women's health products

Increased scale and platform

for growth

Resources to invest in future  
pipeline and strong franchise  
management opportunities

Stronger, enhanced  
management team  
Projected Financial Benefits

Accretive transaction  
1

Revenues >\$475M  
and cash flow >\$200M in  
first 12 months

Strong balance sheet  
with no debt

Lower combined tax rate  
1

Accretion for Jazz Pharmaceuticals shareholders is on a fully-taxed adjusted EPS basis. Adjusted EPS is a non-GAAP financial  
Compelling Strategic and Financial Benefits

Jazz  
Pharmaceuticals plc  
Ireland

Azur Pharma  
Compelling Fit with Jazz Pharmaceuticals  
22  
CNS  
Women's  
Health  
Net Sales (Millions)



Strong commercial focus and expertise  
in CNS and women's health

Approximately 170 employees:

105 people in 3 US sales forces  
across pain, psychiatry and  
women's health

16 person medical affairs team

50 people in home office  
(18 Dublin; 32 Philadelphia)

Pipeline of line extensions for clozapine  
franchise

1.  
Based on estimate provided on September 19, 2011. The estimate is not being updated.

\$5  
\$24  
\$57  
\$67  
\$83  
\$95-100  
Total Net  
Sales  
Estimate  
\$100  
\$80  
\$60  
\$40  
\$20  
\$0  
2006  
2007  
2008  
2009  
2010  
2011  
1

Prialt -  
for Chronic Pain

2010 net sales of \$20M (marketed by Azur since May 2010)

Only  
non-opioid

intrathecal  
(IT)  
analgesic  
for  
severe  
chronic  
pain  
1

Compelling growth opportunity with similar characteristics to Xyrem:

Requires high touch sales capability with heavy clinical emphasis

Currently used in less than 3% of available pain market pumps (approximately 1500)

Limited competitive threats and multiple years of patent and other protection

European rights licensed to Eisai; Azur retains ROW rights

23

1. See full prescribing information on website

FazaClo  
for Treatment Resistant Schizophrenia

2010 net sales of \$37M

Orally disintegrating clozapine tablets approved for management of treatment resistant schizophrenia

1

Approximately 10% prescription share despite largely generic clozapine market

FazaClo High Dose (HD) launched September 2010

More than 27% switched from Low Dose (LD) as of 3Q11

Dosing flexibility and lower pill burden

Generics

filed

to

FazaClo

settlement

with

Teva

with

potential

launch

of

lower

dosage

product in July 2012 and HD in 2015

Additional clozapine line extensions in development

24

1. See full prescribing information on website

25

Diversified and balanced set of six products

1

with 2010 net sales of \$27M

Significant growth opportunity driven by Elestrin

## 1, a topical gel ERT therapy

Patents through 2022

Revamped Elestrin promotion model in 2010 leveraging ~ 50 sales representatives

0%

20%

40%

60%

80%

100%

2009

2010

2011E

Women's Health Products -

Targeting a Growing Market

Elestrin

Other Women's Health

Net Sales Contribution

1. See full prescribing information on website

26  
2011 Estimated Net Sales  
Stand Alone Jazz Pharmaceuticals, Inc.  
Pro forma Jazz Pharmaceuticals plc  
A Growing, Diversified Product Portfolio  
Luvox CR  
13%



Xyrem 87%  
Xyrem 63%  
Luvox CR  
9%  
Prialt 6%  
Women s  
Health 10%  
Other CNS  
1%  
FazaClo LD  
8%  
FazaClo HD  
3%

27

Transaction Closing on Track  
SEC filings and  
stockholder meeting  
Transaction expected  
to close January 2012  
Transaction subject

to customary closing  
conditions and  
regulatory approvals

Azur approval of other  
necessary actions required

US antitrust clearance  
pending

Transaction taxable to Jazz  
Pharmaceuticals, Inc.  
stockholders

Jazz Pharmaceuticals plc shares  
to be traded on Nasdaq under  
**JAZZ**

Azur Pharma S-4 declared  
effective

Proxy statement/prospectus  
mailed to Jazz Pharmaceuticals,  
Inc. stockholders in November

Jazz Pharmaceuticals, Inc.  
stockholder meeting on  
December 12, 2011

28

Strategic Benefits

Diversified portfolio of CNS and  
women's health products

Increased scale and platform

for growth

Resources to invest in future  
pipeline and strong franchise  
management opportunities

Stronger, enhanced  
management team  
Projected Financial Benefits

Accretive transaction  
1

Revenues >\$475M  
and cash flow >\$200M in  
first 12 months

Strong balance sheet  
with no debt

Lower combined tax rate  
1

Accretion for Jazz Pharmaceuticals shareholders is on a fully-taxed adjusted EPS basis. Adjusted EPS is a non-GAAP financial  
Compelling Strategic and Financial Benefits

Jazz  
Pharmaceuticals plc  
Ireland



30

2011G

1

2010

Reconciliation of GAAP Net Income and EPS to Adjusted  
Net Income and EPS in Financial Results and Guidance

(In millions, except per share amounts)

GAAP net income

Add:

Intangible asset amortization

Stock-based compensation expense

Non-cash interest expense and extinguishment of debt

Azur Pharma transaction related costs

Deduct:

Contract revenues

GAAP net income per diluted share (EPS)

Adjusted net income per diluted share (EPS)

Shares used in computing GAAP and adjusted net  
income per diluted share amounts

Adjusted net income

Luvox CR revenue recognition timing change

(1)

\$128-131M

7

13

2

\$160-163

\$2.76-2.81

\$3.45-3.50

46-47

10-11

(1)

\$33

8

8

14

\$61

\$0.83

\$1.55

39

(1)

1.

Based on guidance provided on November 1, 2011. The company is not updating the prior guidance and actual results may dif

-

-



31  
Xyrem  
(sodium oxybate)  
Boxed Warning  
XYREM (sodium oxybate) PI  
!WARNING:  
Central

nervous  
system  
depressant  
with  
abuse  
potential.

Should

not

be

used

with

alcohol

or

other

CNS

depressants.

Sodium oxybate is GHB, a known drug of abuse. Abuse has been associated with some important central nervous system (CNS) adverse events (including death). Even at recommended doses, use has been associated with confusion, depression and other neuropsychiatric events. Reports of respiratory depression occurred in clinical trials. Almost all of the patients who received sodium oxybate during clinical trials were receiving CNS stimulants.

Important CNS adverse events associated with abuse of GHB include seizure, respiratory depression and profound decreases in

level

of

consciousness,

with

instances

of

coma

and

death.

For

events

that

occurred

outside

of

clinical

trials,

in

people

taking

GHB

for

recreational

purposes,

the

circumstances

surrounding

the

events  
are  
often  
unclear  
(e.g.,  
dose  
of  
GHB  
taken,  
the  
nature and amount of alcohol or any concomitant drugs).

Xyrem  
is  
available  
through  
the  
Xyrem  
Success  
Program,  
using  
a  
centralized  
pharmacy  
1-866-XYREM88  
®  
(1-866-997-3688).

The  
Success  
Program  
provides  
educational  
materials  
to  
the  
prescriber  
and  
the  
patient  
explaining  
the  
risks  
and  
proper  
use  
of

sodium oxybate, and the required prescription form. Once it is documented that the patient has read and/or understood the materials, the drug will be shipped to the patient. The Xyrem Success Program also recommends patient follow-up every 3 months. Physicians are expected to report all serious adverse events to the manufacturer. (See WARNINGS).

Luvox CR  
(fluvoxamine maleate)

Boxed Warning

LUVOX CR (fluvoxamine maleate ) PI

Suicidality and Antidepressant Drugs

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term

studies of major depressive disorder (MDD) and other psychiatric Extended-Release Capsules or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. LUVOX CR Capsules are not approved for use in pediatric patients. (See WARNINGS: Clinical Worsening and Suicide Risk, PRECAUTIONS: Information for Patients, and PRECAUTIONS: Pediatric Use.) disorders.

Anyone  
considering  
the  
use  
of  
LUVOX  
CR  
®  
(fluvoxamine  
maleate)

Prialt

(ziconotide intrathecal infusion)

Boxed Warning

Severe psychiatric symptoms and neurological impairment may occur during treatment with PRIALT. Patients with a pre-existing history of psychosis should not be treated with PRIALT. All patients should be monitored frequently

for  
evidence  
of  
cognitive  
impairment,  
hallucinations,

or  
changes  
in

mood or consciousness. PRIALT therapy can be interrupted or discontinued abruptly without evidence of withdrawal effects in the event of serious neurological or psychiatric signs or symptoms

Prialt (ziconotide intrathecal infusion) PI

WARNING:

FazaClo  
(clozapine)

Boxed Warning

1. AGRANULOCYTOSIS

BECAUSE OF A SIGNIFICANT RISK OF AGRANULOCYTOSIS, A POTENTIALLY LIFE-THREATENING ADVERSE CLOZAPINE SHOULD BE RESERVED FOR USE IN (1) THE TREATMENT OF SEVERELY ILL PATIENTS WITH SCHIZOPHRENIA WHO FAIL TO SHOW AN ACCEPTABLE RESPONSE TO ADEQUATE COURSES OF STANDARD



ANTIPSYCHOTIC DRUG TREATMENT, OR (2) FOR REDUCING THE RISK OF RECURRENT SUICIDAL BEHAVIOR IN PATIENTS WITH SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER WHO ARE JUDGED TO BE AT RISK OF REEXPERIENCING SUICIDAL BEHAVIOR. PATIENTS BEING TREATED WITH CLOZAPINE MUST HAVE A BASE

WHITE

BLOOD

CELL

(WBC)

COUNT

AND

ABSOLUTE

NEUTROPHIL

COUNT

(ANC)

BEFORE INITIATION OF TREATMENT

AS WELL AS REGULAR WBC COUNTS AND ANC<sub>s</sub> DURING TREATMENT AND FOR AT LEAST 4 WEEKS

AFTER DISCONTINUATION OF TREATMENT. (SEE WARNINGS.) CLOZAPINE IS AVAILABLE ONLY THROUGH

DISTRIBUTION SYSTEM THAT ENSURES MONITORING OF WBC COUNTS AND ANC<sub>s</sub> ACCORDING TO THE

SCHEDULE

DESCRIBED

BELOW

PRIOR

TO

DELIVERY

OF

THE

NEXT

SUPPLY

OF

MEDICATION. (SEE WARNINGS.)

## 2. SEIZURES

SEIZURES HAVE BEEN ASSOCIATED WITH THE USE OF CLOZAPINE. DOSE APPEARS TO BE AN IMPORTANT

PREDICTOR OF SEIZURE, WITH A GREATER LIKELIHOOD AT HIGHER CLOZAPINE DOSES. CAUTION SHOULD

BE USED WHEN ADMINISTERING CLOZAPINE TO PATIENTS HAVING A HISTORY OF SEIZURES OR OTHER

PREDISPOSING FACTORS. PATIENTS SHOULD BE ADVISED NOT TO ENGAGE IN ANY ACTIVITY WHERE SUDDEN

LOSS OF CONSCIOUSNESS COULD CAUSE SERIOUS RISK TO THEMSELVES OR OTHERS. (SEE WARNINGS.)

## 3. MYOCARDITIS

ANALYSES OF POSTMARKETING SAFETY DATABASES SUGGEST THAT THAT CLOZAPINE IS ASSOCIATED WITH

AN INCREASED RISK OF FATAL MYOCARDITIS, ESPECIALLY DURING, BUT NOT LIMITED TO, THE FIRST

MONTH

OF

THERAPY.

IN

PATIENTS

IN

WHOM

MYOCARDITIS

IS

SUSPECTED,

CLOZAPINE TREATMENT SHOULD BE

PROMPTLY DISCONTINUED. (SEE WARNINGS.)

FazaClo (clozapine) PI  
WARNING:

FazaClo  
(clozapine)  
Boxed Warning -  
continued  
4. OTHER  
ADVERSE  
CARDIOVASCULAR

AND  
RESPIRATORY  
EFFECTS  
ORTHOSTATIC  
HYPOTENSION,  
WITH  
OR  
WITHOUT  
SYNCOPE,  
CAN  
OCCUR  
WITH  
CLOZAPINE TREATMENT. RARELY,  
COLLAPSE CAN BE PROFOUND AND BE ACCOMPANIED BY RESPIRATORY AND/OR CARDIAC ARREST.  
ORTHOSTATIC HYPOTENSION IS MORE LIKELY TO OCCUR DURING INITIAL TITRATION IN ASSOCIATION WITH  
DOSE  
ESCALATION.

IN  
PATIENTS  
WHO  
HAVE  
HAD  
EVEN  
A  
BRIEF  
INTERVAL  
OFF CLOZAPINE (ie, 2 OR MORE DAYS  
SINCE THE LAST DOSE) TREATMENT SHOULD BE STARTED WITH 12.5 MG ONCE OR TWICE DAILY. (SEE WARNINGS  
AND DOSAGE AND ADMINISTRATION.) SINCE COLLAPSE, RESPIRATORY ARREST, AND CARDIAC ARREST DURING  
INITIAL TREATMENT HAS OCCURRED IN PATIENTS WHO WERE BEING ADMINISTERED BENZODIAZEPINES OR  
OTHER PSYCHOTROPIC DRUGS, CAUTION IS ADVISED WHEN CLOZAPINE IS INITIATED IN PATIENTS TAKING  
BENZODIAZEPINE OR ANY OTHER PSYCHOTROPIC DRUG. (SEE WARNINGS.)

5.  
INCREASED  
MORTALITY  
IN  
ELDERLY  
PATIENTS  
WITH  
DEMENTIA-RELATED  
PSYCHOSIS  
ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS TREATED WITH ANTIPSYCHOTIC DRUGS ARE AT  
INCREASED RISK OF DEATH. ANALYSES OF SEVENTEEN PLACEBO-CONTROLLED TRIALS (MODAL DURATION OF  
WEEKS),  
LARGELY  
IN  
PATIENTS  
TAKING  
ATYPICAL  
ANTIPSYCHOTIC

DRUGS,  
REVEALED A RISK OF DEATH IN  
DRUG-TREATED PATIENTS OF BETWEEN 1.6 TO 1.7 TIMES THE RISK OF DEATH IN PLACEBO-TREATED PATIENTS  
OVER THE COURSE OF A TYPICAL 10-WEEK CONTROLLED TRIAL, THE RATE OF DEATH IN DRUG-TREATED  
PATIENTS  
WAS  
ABOUT  
4.5%,  
COMPARED  
TO  
A  
RATE  
OF  
ABOUT  
2.6%  
IN  
THE  
PLACEBO GROUP. ALTHOUGH THE  
CAUSES OF DEATH WERE VARIED, MOST OF THE DEATHS APPEARED TO BE EITHER CARDIOVASCULAR (eg,  
FAILURE,  
SUDDEN  
DEATH)  
OR  
INFECTIOUS  
(eg,  
PNEUMONIA)  
IN  
NATURE.  
OBSERVATIONAL STUDIES SUGGEST  
THAT, SIMILAR TO ATYPICAL ANTIPSYCHOTIC DRUGS, TREATMENT WITH CONVENTIONAL ANTIPSYCHOTIC  
MAY INCREASE MORTALITY. THE EXTENT TO WHICH THE FINDINGS OF INCREASED MORTALITY IN  
OBSERVATIONAL STUDIES MAY BE ATTRIBUTED TO THE ANTIPSYCHOTIC DRUG AS OPPOSED TO SOME  
CHARACTERISTIC(S)  
OF  
THE  
PATIENTS  
IS  
NOT  
CLEAR.  
FAZACLO®  
(clozapine, USP) IS NOT APPROVED FOR THE  
TREATMENT OF PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS. (SEE WARNINGS.)  
FazaClo (clozapine) PI

