



Zyprexa Global Issues

Opportunity/Issues/Competition

October 14-15, 1998



Competitive Update

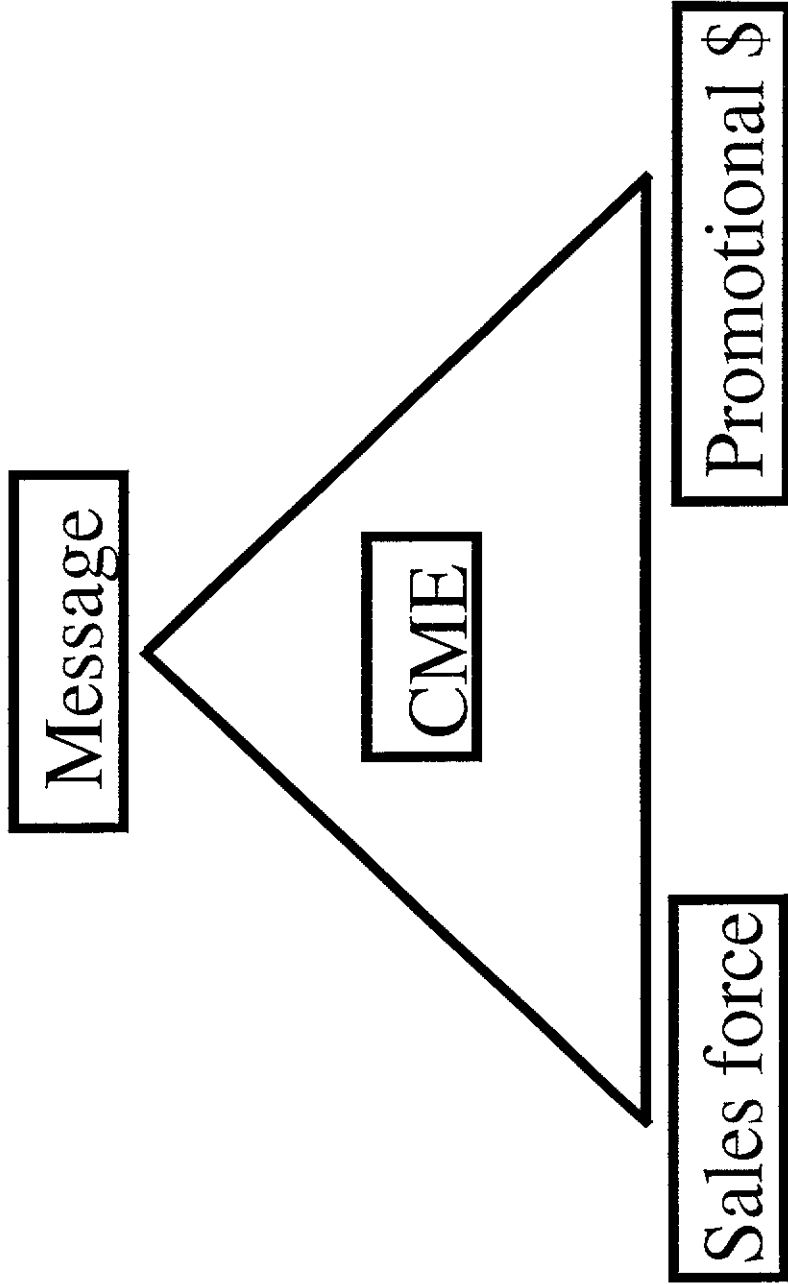
Focus on Risperdal
& Zotepine Profile

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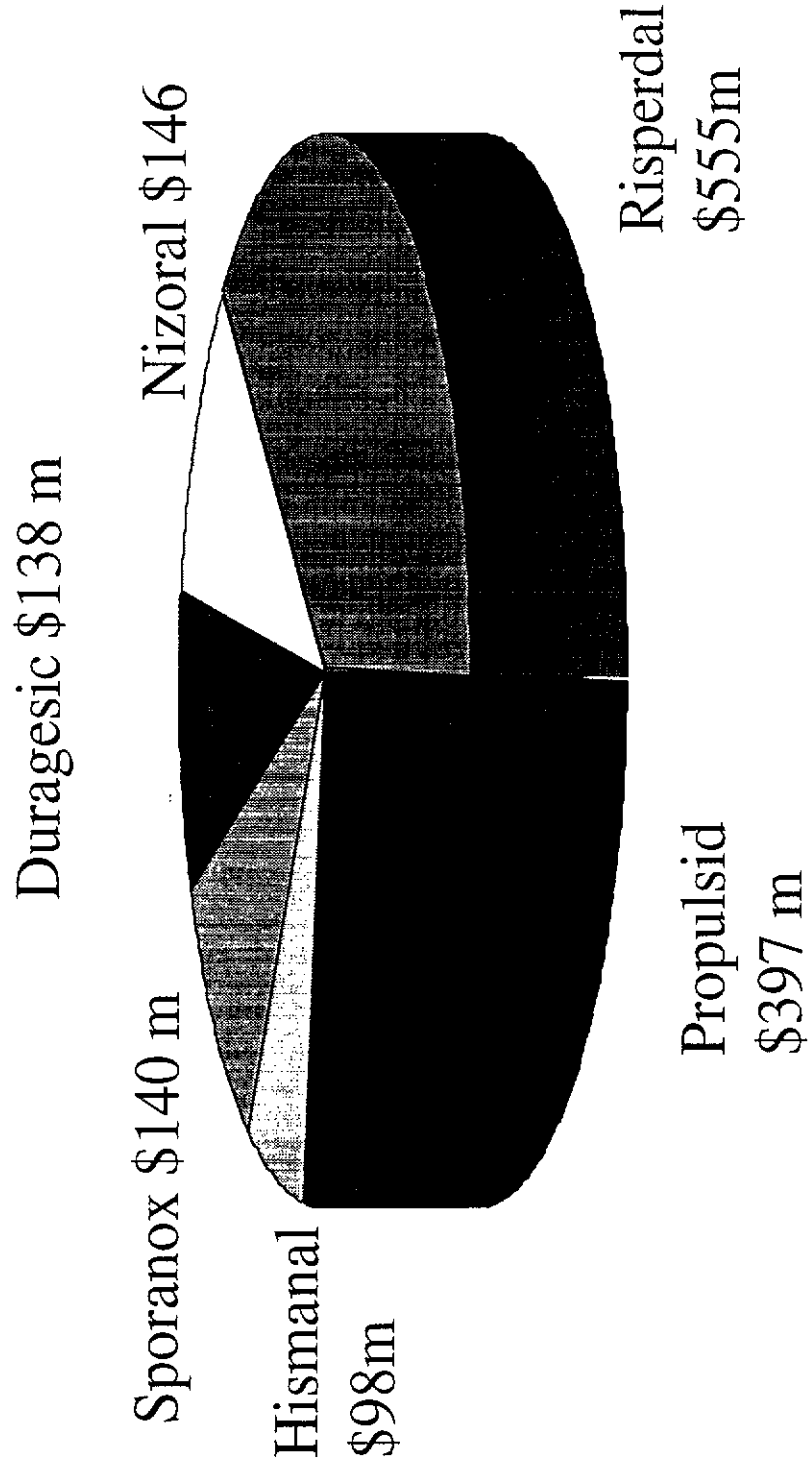
Janssen, US Promotional Mix

- Janssen Sales Performance





Janssen '97 US sales



Janssen Product Portfolio

US Sales

ZY 2153 1067

<u>Product</u>	<u>Class</u>	<u>'97 sales</u>
Risperdal	anti-psychotic	\$555M
Propulsid	anti-ulcer	\$397 M
Sporanox	anti-fungal	\$140 M
Duragesic	analgesic	\$138 M
Nizoral	anti -fungal	\$146M
Hismanal	antihistamine	\$98 M



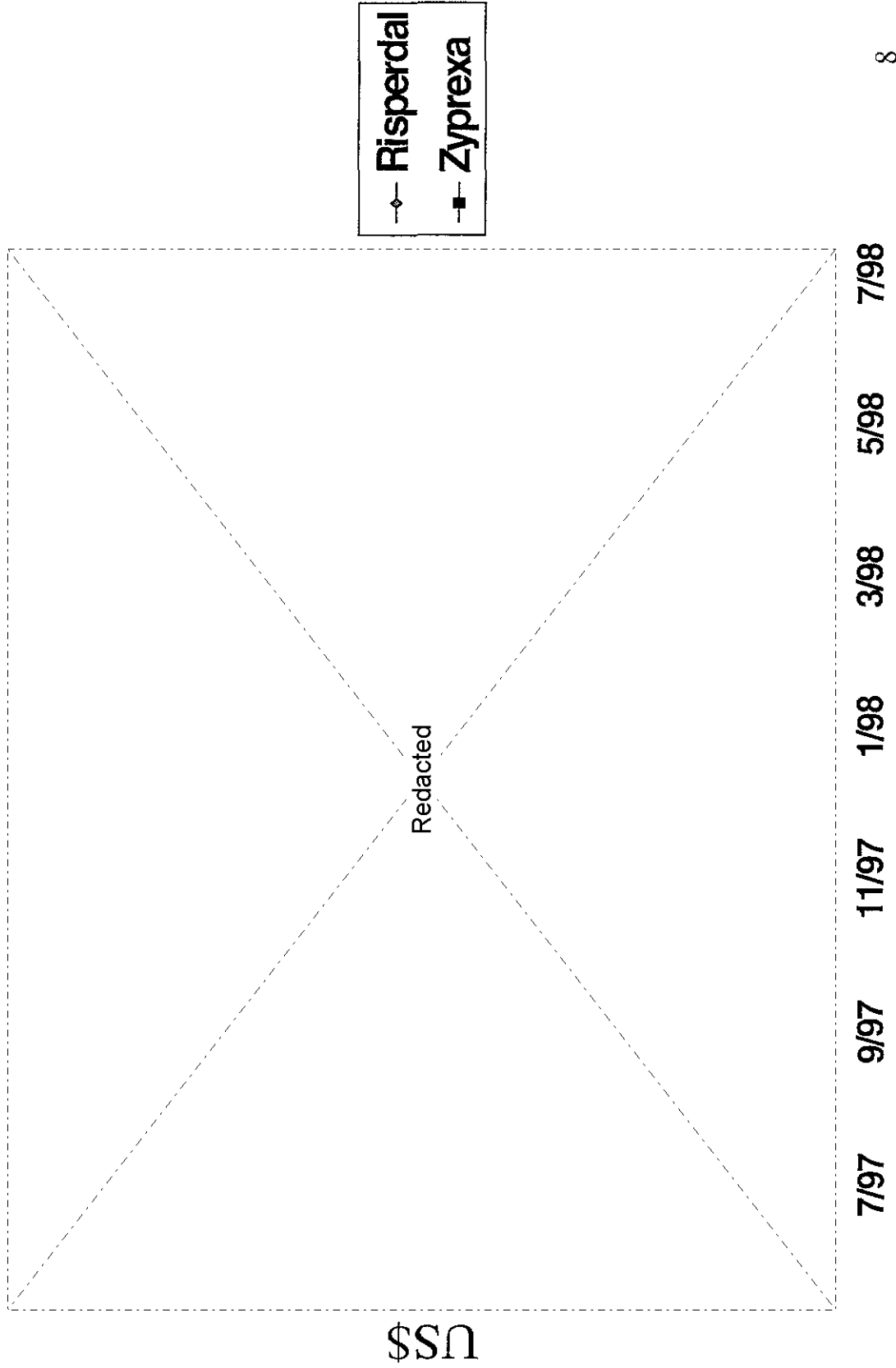
Janssen US Risperdal Message

- "Rethink Risperdal"
 - Schizophrenia, Bipolar, Elderly psychosis
- Positive and negative symptoms + *safety profile and cognitive function benefits that help redefine efficacy*
 - Impaired cognition can affect...
 - Impaired cognition may be associated with...
 - Low risk of anticholinergic side effects and their impact on cognitive function...Zyprexa...
- Weight gain - lack of it may encourage compliance
- Cost - 2, 4, 6mg Vs. 10, 15, and 20mg Zyprexa

Janssen US Risperdal Message

- Person to Person - patient compliance & support
- Dosing flexibility (initial dosing for acute to chronic patients - 1mg BID, titrate at daily to weekly intervals, now approved in QD dosing)
- Benefits for the elderly
 - Low EPS
 - sedation
- Receptor profiles
 - Zyprexa high M₁, H₁, and α_1 affinity

Risperdal Vs. Zyprexa Promotional Spend



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Janssen CME program - 4/25/98

- Efficacy of 6mg Risperdal superior to 20mg Haldol for + and - sx's
- Efficacy of 15mg Zyprexa superior to Haldol for - sx's, **not superior** on + sx's
- Co-prescription of typicals:
 - Zyprexa, 22% of pts Risperdal, 6%
 - (Data from "US psychs")*
- Average dose for schizophrenia:
 - Zyprexa, 15.7mg Risperdal, 4.1mg

Risperdal superior for both + and - sx's, Zyprexa only for -, which may explain higher rate of adjunctive typical use



Janssen CME Program

- Treatment Resistant Schizophrenia:
 - Risperdal 6mg equal to Clozaril (150-400mg)
 - No difference in EPS
 - Zyprexa 25mg not superior to Thorazine
 - Less EPS with Zyprexa
 - “*titrating up to 40mg, see how it goes*”

Clozaril is the Gold Standard for TX resistant pts -
Risperdal proven equally effective



Janssen CME Program

- Bipolar Disorder
 - Atypicals may possess Mood Stabilizing Properties
 - Risperdal 2-3mg/day, 65-85% response rate, mostly as an adjunct to a M.S. (*open label reports*)
 - Rationale for Risperdal ‘inducing’ mania = pts were withdrawn from their M.S.
 - Zyprexa trials : 48.6% total response vs 24.2% placebo

**Monotherapy with an atypical for Bipolar is
NOT AN APPROPRIATE STRATEGY**



Janssen CME Program

- Dementia
 - Risperdal being used 1st line in the US
 - Start at 1/4mg and titrate up to 1 or 2mg
 - Zyprexa 1-8mg/day not superior to placebo, “*maybe the dose was too low*”
 - Study in elderly schizophrenics showed Zyprexa = Haldol on efficacy and disc rates

Risperdal has by far the most data in elderly -
Dementia and Schizophrenia

Janssen CME Program



- EPS for Risperdal dose dependent but only above 8mg
- Rationale for *occasional* EPS at lower doses = 10% of pts are deficient in isoenzyme that metabolizes Risperdal
- Zyprexa, superiority to Haldol shown at at lower doses but not 15mg or above
- Seroquel - best EPS profile

EPS profiles of Zyprexa and Risperdal are similar



Janssen CME Program

- Zyprexa, Clozaril, Seroquel = most H1 blockade
- Weight gain has serious consequences - 'diet modification' is not a satisfying answer for these pts
- Verbalized that Zyprexa = Clozaril in wt gained, takes 6 mos to plateau
- Risperdal gains take 3 mos to plateau

Zyprexa and Clozaril have similar wt gain profiles - can lead to greater risk of CV disease, diabetes, etc.



Janssen CME Program

- All antipsychotics have potential to increase prolactin
- Risperdal - no significant correlation with side effects in males or females
- Seroquel and Clozaril least likely to elevate levels
 - switch to one of them if side effects '*happen to occur*' with Risperdal

Risperdal has greatest potential to elevate prolactin
but most patients will not suffer side effects



Janssen CME Program

- 85% schizophrenics meet clinical criteria for cognitive impairment
- Cognitive deficits contribute significantly to long term disability (prevent 'reintegration')
- Atypicals may provide a *primary* benefit of improving cognition
- Limited data exists

More studies need to be done, but most impressive data currently is with Risperdal



Janssen US Sales Force

<u>Division</u>	<u># of reps</u>	<u>Products</u>
Janssen Field 1	500	Sporanox, Propulsid
Janssen Field 2	425	Propulsid, Sporonox
CNS	150	Risperdal, Paxil
Janssen Hosp.	110	Sporonox, Propulsid, Duragesic

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Zotepine Profile

Zotepine, Lodopin, Nipolept (Fujisawa, Knoll, Klinge/ RPR - Germany)

- D₁, D₂, 5HT₂ antagonist, and norepinephrine uptake inhibitor
- Launched: Austria, Germany, Japan, and South Korea
- Preregistered: France, Spain, Taiwan, and the UK (Mutual recognition process initiated*)
- Indication: Treatment of schizophrenia
- Dose: 150 - 300 mg
- Claims: Statistically superior to chlorpromazine (BPRS), relapse prevention (double blind placebo controlled), with low EPS
- Other: Undergoing clinical trials in Germany for Manic disorders
- Weaknesses: Negative Sx efficacy questionable, prolactin elevation, seizures



Risperdal Competitive Strategy Session (US)

Threats and Opportunities for
Zyprexa

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Risperdal Competitive Strategy Session

Top threats to Zyprexa

ZY 2153 1082

- Weight gain
 - Need for framing from outside opinion leaders
 - Acknowledge issue, characterize as class effect, and put it in perspective
- Cognition
 - Complex issue, first address peer to peer
 - Question validity of Janssen claims

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Risperdal Competitive Strategy Session

Top threats to Zyprexa, cont.

ZY 2153 1083

- Elderly
 - Janssen effectively using elderly data in market segments that we are not currently pursuing
 - Lilly LTC sales force is out numbered and ineffective
- Cost/Dose
 - Slow onset of action an issue (acute care)
 - Needs to be framed as total cost issue
 - 4mg Risperdal not effective
 - Time/dose study needed for 10 - 15 mg separation

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● US Affiliate Action Steps

Zyprexa's Opportunities



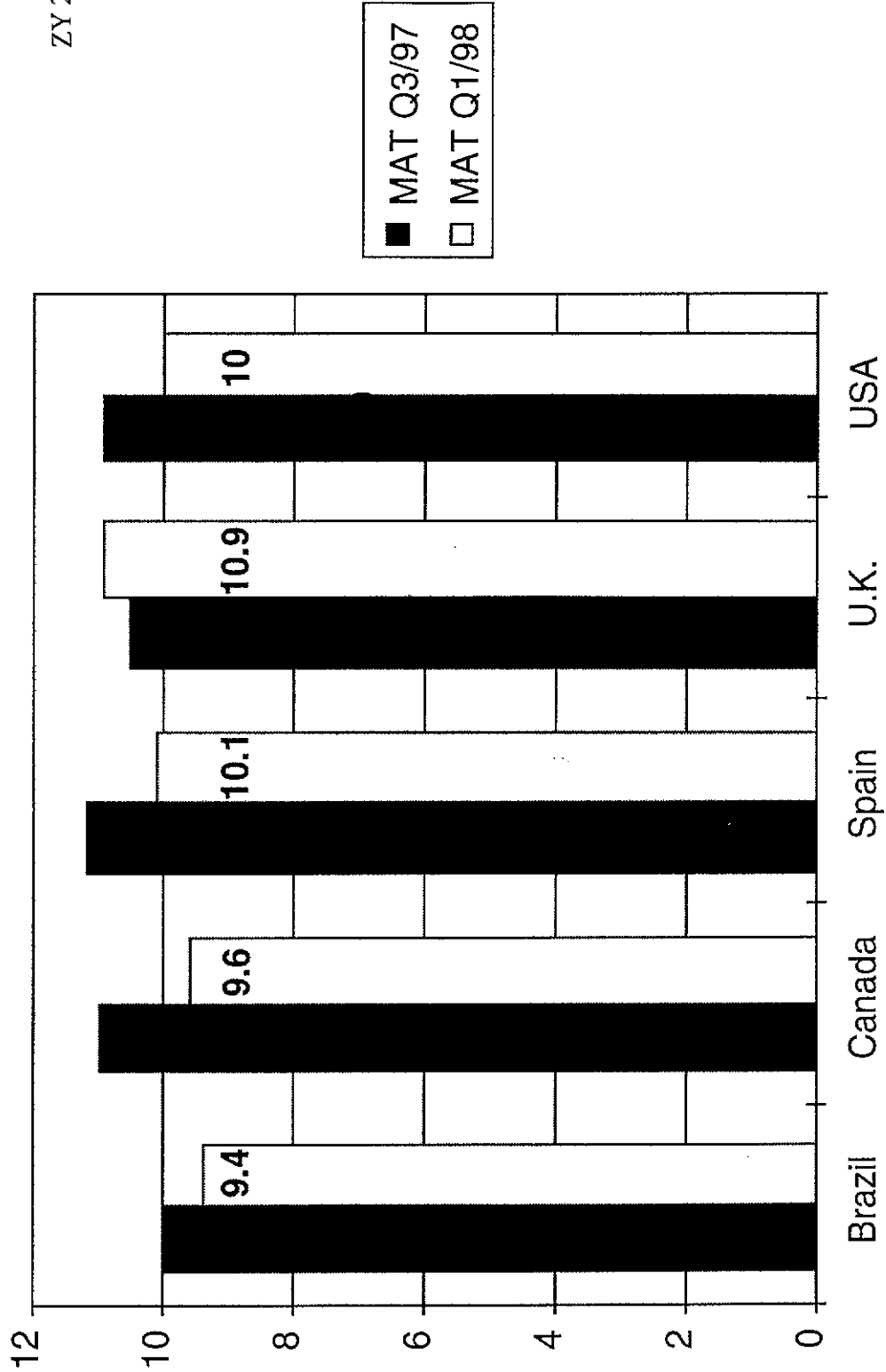
- Higher patient functioning is the major differentiator for Zyprexa
- Market segmentation business case needed - Is the elderly market (22.5%) worth it?
- Tone is crucial - handle objections and get back to selling
- Analysis of strategic pricing options needed - High strength tablets

Zyprexa Dose

All Diagnoses



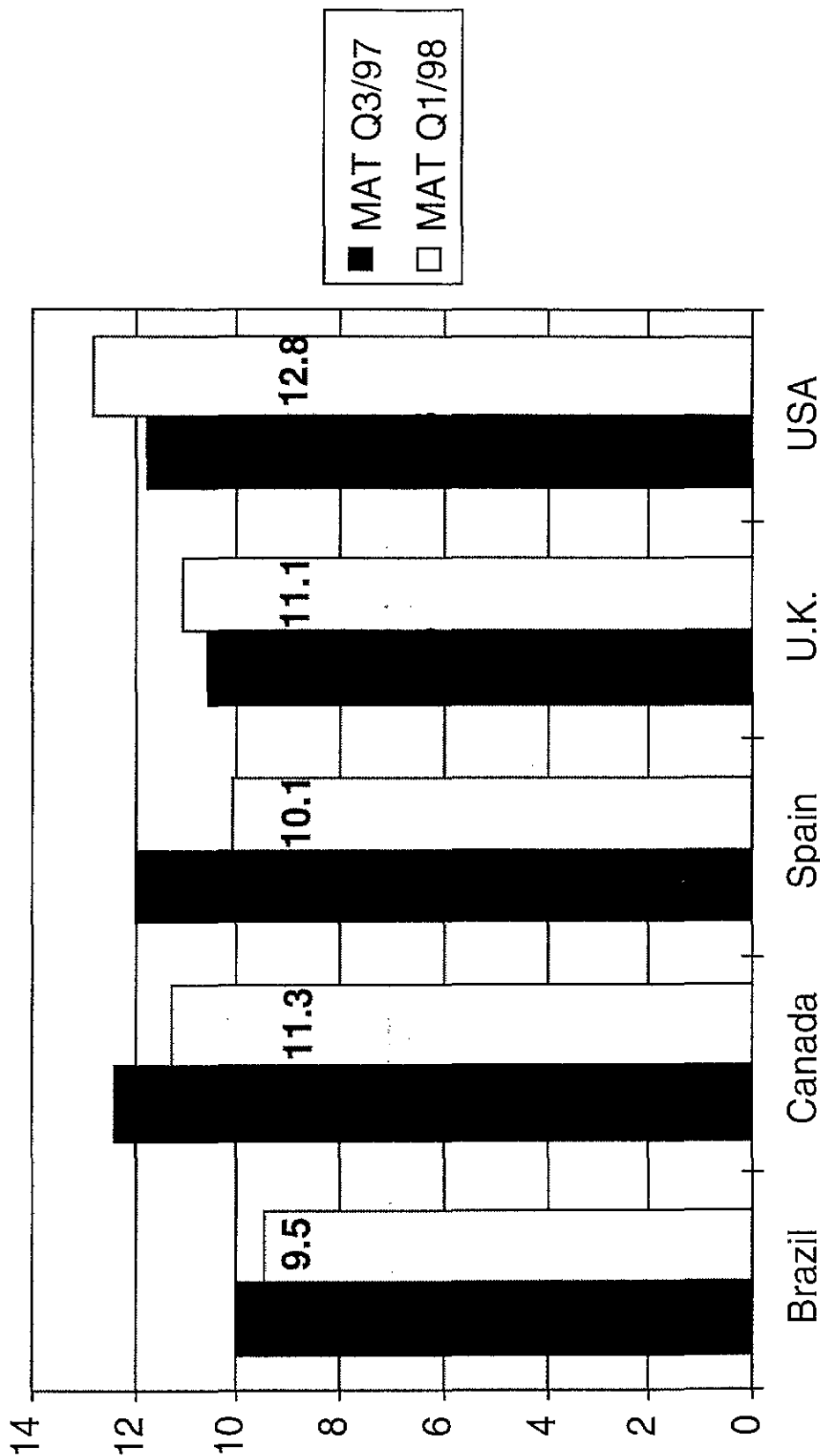
ZY 2153 1085



Source: IMS Med. Midas

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Zyprexa Dose Schizophrenia



Source: IMS Med. Midas

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