

	ok	ok	ok	ok		
Fluoxetine Originator vs Generic Package Inserts						
	Prozac (Originator) Eli Lilly	Lilly: fluoxetine (Eli Lilly)	ProHexal (Hexal)	Nuzak (Cipla)	Lorien (Pharma-care)	Sandoz: Fluoxetine
1. INDICATIONS						
Major depressive episodes (single episodes & recurrent depression with associated anxiety)	x	x	x	x	x	x
Bulimia nervosa - decrease binge-eating and purging	x	x	x	x	x	x
Obsessive-compulsive disorder (intrusive, markedly distressing, time consuming or significant functional interference)	x	x	x	x	x	x
Total	3	3	3	3	3	3
p=Proportion		p= 3/3=100	p=3/3=100	p=3/3=100	p=3/3=100	p=3/3=100
2. RECOMMENDED DOSAGE						
Oral administration to adults only	x	x	N	x	x	x
Major depressive episode: 20 mg per day, preferably in the morning. Doses above 80 mg per day not recommended	x	x	x	x	x	x
Bulimia nervosa: 60 mg per day	x	x	x	x	x	x
Obsessive-compulsive disorder: 20 - 60 mg per day	x	x	x	x	x	x
With or without food	x	x	x	x	x	x
Tablets swallowed whole or dispersed in 100 ml water	x	N	x	N	x	N
Elderly: Use with caution esp with systemic illness or multiple medication	x	x	x	x	x	N
Total	7	6	6	6	7	5
p=Proportion		p=6/7=86	p=6/7=86	p=6/7=86	p=7/7=100	5/7=71
3. CAUTIONS						
Warnings						
Rash and possibly allergic phenomena - discontinue fluoxetine	x	x	x	x	x	N
Total	1	1	1	1	1	0
p=Proportion		p=1/1=100	p=1/1=100	1/1=100	p=1/1=100	p=0/1=0.00
Contra-indications						
Hypersensitivity to any of the ingredients	x	x	x	x	x	x
Severe renal failure (GFR < 10 ml/min)	x	x	x	x	x	x
MAOI's during therapy or within 14 days of discontinuing MAOI's. Start MAOI's only 5 weeks after stopping fluoxetine	x	x	x	x	x	x
Pregnancy	x	x	x	x	x	x
Breastfeeding	x	x	x	x	x	x
Children	x	x	x	x	x	x
Total	6	6	6	6	6	6
p=Proportion		p=6/6=100	p=6/6=100	p=6/6=100	p=6/6=100	p=6/6=100
Special precautions						
Seizures	x	x	x	x	x	x
Avoid in unstable epilepsy	x	x	N	x	x	N
Careful monitoring of patients with controlled epilepsy	x	x	N	N	x	N
Prolonged seizures in pts receiving ECT therapy	x	x	N	x	x	N
Lower or alternate day dosing in significant hepatic dysfunction or mild to moderate renal failure (GFR 10-50 ml/min)	x	x	x	x	x	x
Acute cardiac disease - caution due to lack of clinical experience	x	x	x	x	x	N
Loss of body mass	x	x	x	x	x	x
Altered glycaemic control in diabetics - hypoglycaemia during & hyperglycaemia after stopping fluoxetine	x	x	x	x	x	x
Altered platelet function	x	x	N	x	x	N
Abnormal bleeding	x	x	N	x	x	N
Impairment of judgement or skills eg. Caution of impaired ability to perform potentially harmful tasks, eg. Driving & operating mach	x	x	x	x	x	x
Improvement may be only after 2-3 weeks, therefore supervision of high suicide risk patients is necessary	x	x	N	x	x	x
Observe same precautions for depressive & obsessive-compulsive patients	x	x	N	x	x	N
Total	13	13	6	12	13	6
p=Proportion		p=13/13=100	p=6/13=46	p=12/13=92	p=13/13=100	6/13=46
Overall Cautions	20	20	12	19	20	12
	p=20/20=100	p=12/20=60	19/20=95	20/20=100	p=12/20=60	
4. SIDE-EFFECTS						
Asthenia	x	x	x	x	x	x
Fever	x	x	x	x	x	x
Palpitations	x	x	x	x	x	x
Vision disturbances	x	x	x	x	x	x
Nausea	x	x	x	x	x	x
Diarrhoea	x	x	x	x	x	x

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Dry mouth	x	x	x	x	x	x
Appetite loss	x	x	x	x	x	x
Dyspepsia	x	x	x	x	x	x
Vomiting	x	x	x	x	x	x
Headache	x	x	x	x	x	x
Nervousness	x	x	x	x	x	x
Insomnia	x	x	x	x	x	x
Drowsiness	x	x	x	x	x	x
Anxiety	x	x	x	x	x	x
Tremor	x	x	x	x	x	x
Dizziness	x	x	x	x	x	x
Fatigue	x	x	x	x	x	x
Decreased libido	x	x	x	x	x	N
Seizures	x	x	x	x	x	x
Hypomania or mania	x	x	x	N	x	x
Abnormal dreams	x	x	x	x	x	x
Agitation	x	x	x	x	x	x
Dyspnoea	x	x	x	x	x	x
Pulmonary events incl inflam process with varying histopathology and/or fibrosis	x	x	x	x	x	x
Rash	x	x	x	x	x	x
Urticaria	x	x	x	x	x	x
Serious systemic events poss related to vasculitis, and rarely death	x	x	x	x	x	x
Excessive sweating	x	x	x	x	x	x
Serum sickness	x	x	x	x	x	N
Anaphylactoid reactions	x	x	x	x	x	N
Sexual dysfunction (delayed or inhibited orgasm)	x	x	x	x	x	x
Hypothyroidism	x	x	x	x	x	x
Hyponatraemia	x	x	x	x	x	x
Elevated serum transaminase	x	x	x	x	x	N
Aplastic anaemia	x	x	x	x	x	x
Cerebral vascular accident	x	x	x	x	x	x
Confusion	x	x	x	x	x	x
Dyskinesia	x	x	x	x	x	x
Echymoses	x	x	x	x	x	N
Eosinophilic pneumonia	x	x	N	x	x	x
Gastro-intestinal haemorrhage	x	x	x	x	x	N
Hyperprolactinaemia	x	x	x	x	x	x
Movement disorders & worsening of pre-existing movement disorders	x	x	x	x	x	x
Neuroleptic malignant syndrome-like events	x	x	x	N	x	x
Pancreatitis	x	x	x	x	x	x
Suicidal ideation	x	x	x	x	x	x
Pancytopenia	x	x	x	x	x	x
Immune-related haemolytic anaemia	x	x	x	x	x	x
Thrombocytopenia	x	x	x	x	x	x
Thrombocytopenic pupura	x	x	x	x	x	x
Vaginal bleeding after withdrawal of the medication	x	x	x	x	x	x
Violent behaviour	x	x	N	x	x	x
Total	53	53	51	51	53	47
p=Proportion		p=53/53=100	p=51/53=96	p=51/53=96	p=53/53=100	47/53=0.89
5. DRUG INTERACTIONS						
MAOI's	x	x	x	x	x	N
CNS active drugs including lithium (increased or decreased lithium levels)	x	x	x	x	x	x
2-fold increase in other anti-dressants blood levels	x	x	x	x	x	x
Adverse events with tryptophan (agitation, restlessness & gastro-intestinal distress)	x	x	x	x	x	x
Long elimination half life of fluoxetine & its metabolites wrt pharmacodynamic or pharmacokinetic drug interactions	x	x	N	x	x	N
Diazepam - half life prolonged	x	x	x	x	x	x
Altered plasma concentrations of other plasma protein bound drugs eg. Warfarin, digitoxin	x	x	x	x	x	x
Fluoxetine plasma binding may be altered by other agents	x	x	x	x	x	x
Total	8	8	7	8	8	6
p=Proportion		p=8/8=100	p=7/8=88	p=8/8=100	p=8/8=100	p=6/8=75
Date of Publication	26/07/1996	Jul-96	Jan-01	May-98	Mar-02	Sep-97

Mean of p values=Overall p value 1.00 +1.00 +1.00+1.00+1.00÷5=1.00

q=1-1=0
pq=0x0=0
Std Deviation= $\sqrt{(pq \div n)} = \sqrt{(0 \div 5)} = \sqrt{0} = 0$
95% CI = $p \pm (2.776 \times \text{Std Dev}) = p \pm (2.776 \times 0) = p \pm 0$
95%CI = 1.0±0 ie. 1.0 to 1.0

Mean of p values=Overall p value 0.86 +0.86 +0.86+1.00+0.71÷5=0.86

q=1-0.86=0.14
pq=0.86x0.14=0.12
Std Deviation= $\sqrt{(pq \div n)} = \sqrt{(0.12 \div 5)} = \sqrt{0.02} = 0.16$
95% CI = $p \pm (2.776 \times \text{Std Dev}) = p \pm (2.776 \times 0.16) = p \pm 0.44$
95%CI = 0.86±0.44 ie. 1.3 to 0.42

Mean of p values=Overall p value 1.00 +0.60 +0.95+1.00+0.60÷5=0.83

q=1-0.83=0.17
pq=0.83x0.17=0.14
Std Deviation= $\sqrt{(pq \div n)} = \sqrt{(0.14 \div 5)} = \sqrt{0.03} = 0.17$
95% CI = $p \pm (2.776 \times \text{Std Dev}) = p \pm (2.776 \times 0.17) = p \pm 0.47$
95%CI = 0.83±0.47 ie. 1.3 to 0.36



Mean of p values=Overall p value 1.00 +0.96 +0.96+1.00+0.89+5=0.96

$q=1-0.96=0.04$
 $pq=0.96 \times 0.04=0.04$
 $\text{Std Deviation}=\sqrt{(pq \times n)}=\sqrt{(0.04 \times 5)}=\sqrt{0.008}=0.09$
 $95\% \text{ CI} = p \pm (2.776 \times \text{Std Dev}) = p \pm (2.776 \times 0.09)=p \pm 0.24$
 $95\% \text{ CI} = 0.96 \pm 0.24 \text{ ie. } 1.2 \text{ to } 0.72$



Mean of p values=Overall p value 1.00 +0.88 +1.00+1.00+0.75+5=0.93

$q=1-0.93=0.07$
 $pq=0.93 \times 0.07=0.07$
 $\text{Std Deviation}=\sqrt{(pq \times n)}=\sqrt{(0.07 \times 5)}=\sqrt{0.01}=0.11$
 $95\% \text{ CI} = p \pm (2.776 \times \text{Std Dev}) = p \pm (2.776 \times 0.11)=p \pm 0.32$
 $95\% \text{ CI} = 0.93 \pm 0.32 \text{ ie. } 1.25 \text{ to } 0.61$