

# Reasons for referral and consultation liaison psychiatry diagnoses

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*Ir J Psych Med* 2010; 27(3): 123-129

## Abstract

**Objectives:** Focused management strategies, including effective distribution of available resources is dependent on ongoing analysis of referral type in any liaison psychiatry consultation service. This survey sought to measure rate of diagnoses in an Irish liaison psychiatry consultation service, and compare the results with other similar services.

**Method:** A survey of referral reasons and diagnoses was performed on all patients presenting to a Dublin based inpatient liaison psychiatry consultation service over two six month periods. The results were subsequently compared with other similar international studies.

**Results:** Commonest referral reasons were for depressive disorders, while commonest diagnoses included alcohol related disorders, depressive disorders, and delirium, with notably higher rates of alcohol related disorders than in other similar international studies.

**Conclusions:** This study provides valuable information for referral reasons and diagnoses present in an Irish liaison psychiatry consultation service. The differences noted between diagnoses in our study and other international studies, as well as some of the difficulties in establishing these diagnoses, are discussed.

**Key words:** Diagnosis; Survey; Liaison psychiatry consultation.

## Introduction

Knowledge of the type of referral received is essential in order to plan for future service need in liaison psychiatry services.<sup>1</sup> It is important to be aware of common diagnoses as part of an evidence based practice model, so that liaison psychiatry services are informed of how common presentations are in a service.

Decision making on funding allocation (for example

employment of an alcohol counsellor in a service) requires basic knowledge of diagnoses within the service, in order to prioritise resources appropriately. Establishing diagnoses also allows for monitoring of possible future trends, and hypothesising for possible reasons for these trends.<sup>2</sup> Furthermore, knowledge of psychiatric co-morbidities in Irish hospitals is useful for educational purposes for the medical and psychiatry community in general.

A number of international studies have identified the types of referral received in liaison psychiatry consultation services (also known as consultation-liaison (C-L) psychiatry services), however following extensive literature review, few studies identified the types of referral seen by inpatient liaison psychiatry consultation services in an Irish setting.

A survey performed by a liaison service in Cork, over 25 years ago, looked at referrals from both the emergency department (150 referrals), and from the general wards (220 referrals).<sup>3</sup> The commonest referral reasons (emergency department and general ward referrals were combined) included assessments for parasuicide or suicidal risk (38%), suspected psychiatric illness (31%), suspected psychosomatic basis for symptoms (11%), and 'past psychiatric history' (6%). The most frequent diagnoses given, based on ICD-9 criteria, included neurotic disorders (44%), alcohol dependence syndrome (10%), personality disorders (10%), functional psychotic disorders (7%), and 'no psychiatric diagnosis' (7%).

The authors noted relatively high rates of referral for alcoholism, as well as for functional psychosis, suggesting that this likely reflected the state of affairs in the community. The reason for the high rate of neurotic disorders is not fully clear, but it is likely that neurotic disorders and affective disorders were combined in this study.

Another study performed in Cork University Hospital in 2003, looked specifically at referrals to the liaison psychiatry consultation service from the neurology department.<sup>4</sup> A total of 6% (106) of all neurology admissions were referred to the liaison psychiatry service, while 20% (327) of all discharge forms had documented psychiatric diagnoses. Common diagnoses satisfying DSM-IV criteria were major depressive disorder (24%), somatoform disorder (23%), alcohol use disorder (20%), adjustment disorder (6%), psychotic disorder (5%), organic mood disorder (5%), and anxiety disorder (5%). Another review from 1991 looked at referrals to an old age psychiatry service only.<sup>5</sup>

## Aim

The aim of this study was to obtain information on the psychiatric diagnoses of patients referred to a liaison psychiatry service, and to compare this with other similar studies performed previously. A second aim was to compare reasons

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SUBMITTED: MAY 21, 2009. ACCEPTED: NOVEMBER 20, 2009.

Table 1: Age and gender

Age	Male n (% total)	Female n (% total)
16-25	19 (5.4)	23 (6.6)
26-35	21 (6)	20 (5.7)
36-45	18 (5.1)	23 (6.6)
46-55	27 (7.7)	40 (11.4)
56-65	38 (10.9)	39 (11.1)
66-75	20 (5.7)	22 (6.3)
>75	18 (5.1)	22 (6.3)
<b>Total</b>	<b>161 (46)</b>	<b>189 (54)</b>

for referral and diagnoses determined by a liaison psychiatry service.

### Study setting

St Vincent's University Hospital is a tertiary referral centre in Dublin, with a capacity of 514 beds. It is the national referral centre for cystic fibrosis and liver transplants. The liaison psychiatry service covers consultation referrals from other medical teams around the hospital, as well as attending to referrals from the emergency department. This survey was restricted to patients seen following admission.

The service consists of one half time consultant liaison psychiatrist, sessions from a second consultant psychiatrist, and three psychiatry registrars, who work in conjunction with a multidisciplinary team.

Referrals to the old age psychiatry team, who see inpatient consultations over the age of 65 years within the catchment area for old age psychiatry for the hospital, were not included. Patients over 65 years outside this catchment area, and those who were previously linked in with a psychiatry service, were seen by the liaison psychiatry team, and are included in this survey.

### Methods

All liaison psychiatry inpatient consultations were recorded in a consultation diary over two six month periods, between 1/7/07-31/12/07, and again between 1/7/08-31/12/08. Patient demographics, referral reason, and clinical diagnoses were documented by the three psychiatry registrars attached to the service. Clinical diagnoses, based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM-IV-TR), were used by registrars, with a similar level of clinical expertise, and with the supervision of two consultant psychiatrists.

All registrars involved were on a psychiatry training scheme, with at least one year experience training in psychiatry. After seeing patients on the medical wards, clinical diagnoses were recorded in the consultation diary, based on the clinical assessment. These diagnoses were subsequently confirmed at meetings between registrars and consultant.

At the end of each six month period there was a retrospective review of the consultation diary, and data was recorded on data collection sheets by the registrars involved. The data obtained was transferred using an Excel spreadsheet into the statistical package STATA 8.2 for tabulation.

A literature search was subsequently performed looking

Table 2 (i): Referral reason and diagnosis by liaison psychiatry service

Diagnostic categories	Referral Reason (%)	Diagnosis (%)
Depressive disorders	101 (28.9)	58 (16.6)
Alcohol related disorders	53 (15.1)	69 (19.7)
Delirium (agitation/confusion included in referral reasons)	46 (13.1)	41 (11.7)
Anxiety disorders	34 (9.7)	32 (9.1)
Psychotic disorders	28 (8.0)	27 (7.7)
Bipolar disorders	14 (4.0)	18 (5.1)
Substance related disorders other than alcohol	13 (3.7)	23 (6.6)
Somatoform disorders	9 (2.6)	10 (2.9)
Eating disorders	5 (1.4)	5 (1.4)
Adjustment disorders	4 (1.1)	25 (7.1)
Personality disorders	2 (0.6)	19 (5.4)
Dementia	0 (0)	6 (1.7)
Other diagnosis	13 (3.7)	5 (1.4)
No psychiatric diagnosis/ Diagnosis deferred	-	26 (7.4)

Table 2 (ii): Other referral reasons and assessment impressions/outcomes

Other referral reasons and outcomes	Referral reason (%)	Assessment impression/outcome (%)
DSH/Risk assessment*	63 (18)	36 (10.3)
Medication/side effect related	24 (6.9)	26 (7.4)
Capacity assessment	15 (4.3)	-
Refused assessment	-	6 (1.7)
Discharged prior to assessment	-	4 (1.1)

\*DSH/Risk assessment referral reason figure includes those referred for risk assessment; assessment impression/outcome figure includes only those who had self-harmed

at similar studies performed previously, mainly focusing on more recent large scale studies, with results being compared between studies. Only studies performed in the last 12 years were included as studies prior to this often used different diagnostic criteria, and hence comparison was more difficult.

As part of the study other quality indicators, including time to consultation for referrals, were also recorded, however this data is not presented in this paper. It should also be noted that the diagnoses present in the first six months of this study has already been presented in a previous paper,<sup>6</sup> however the results in this paper refer to the entire study only. Hospital ethics committee approval was obtained prior to commencing the study.

### Results

A total of 172 patients were referred in the initial survey, and 178 patients in the second survey, giving a total of 350 patients between both surveys. Overall 54% of patients were female and 46% male, with a mean age of 51.2 years (age

range: 16-92 years). The highest portion of referrals for both males and females were for the age groups between 46-65 years (Table 1). There were a total of 15,672 admissions (excluding admissions to the psychiatric unit) to the hospital during the survey, giving a referral rate of 2.2%.

Table 2 (i) illustrates the referral reason by the medical teams and diagnoses given by the liaison psychiatry service. Depressive disorders were the commonest referral reason by far (28.9% of all referrals), while alcohol related disorders were commonly referred also (15.1% of all referrals). Referrals with a query regarding delirium/agitation/confusion were also common (13.1% of total). Other common referrals included anxiety disorders, psychotic disorders, bipolar disorders and substance related disorders other than alcohol.

Table 2 (ii) illustrates other referral reasons and assessment impressions/outcomes. Risk assessment was referral reason for 18% of referrals, and advice regarding medications or side effects of medications was also a common referral reason (6.9%). A total of 75/350 (21.4%) patients had more than one referral reason.

Diagnoses made by the liaison psychiatry service illustrated some differences from the referral reasons. Alcohol related disorders were the commonest diagnosis with 19.7% of all referrals, while depressive disorders were diagnosed in 16.6%. Of the 101 referrals (28.9% of all referrals) for assessment for depressive disorders, 48 were diagnosed with depression, 14 with adjustment disorder, 13 with no psychiatric diagnosis/diagnosis deferred, nine with alcohol/substance use disorders, five with personality disorder, four with delirium, and nine more with various other diagnoses.

Of note, 58 patients were diagnosed with depression in total (Table 2 (i)), however this includes 10 patients referred for reasons other than depression (eg. for risk assessment), who satisfied a diagnosis of depression following consultation.

Delirium, anxiety disorders, psychotic disorders and adjustment disorders were also commonly diagnosed by the liaison psychiatry team in the survey. DSH had occurred in 10.3% of referrals. Of the patients, 40/350 (11.4%) were given more than one diagnosis.

### Review of previous studies

There have been several previous international studies, measuring psychiatric diagnoses in liaison psychiatry consultation services, the results of some of which are presented in Tables 3 (i) and 3 (ii).

We reviewed eight previous research papers, focusing on more recent, large scale studies. Heterogeneity among these studies is evident, with differing diagnostic criteria used, and use of differing diagnostic categories. For example, a number of the research studies combine depressive disorders and bipolar disorders into a single category of affective disorders, and likewise delirium, dementia, and other cognitive disorders were sometimes reported under the single heading of organic mental disorders. A further category which was not reported on consistently was substance related disorders, with only some studies including alcohol related disorders under this heading. Three of these studies involved two separate surveys, meaning 11 studies were looked at in total.

The Irish studies mentioned in the introduction were not included in this comparison, as the only one of these relating

to a general adult liaison psychiatry consultation service was performed in 1986, and utilised ICD-9 criteria, which was difficult to compare to our study. Emergency department and general ward referrals were also combined in this study.<sup>3</sup> We did not find more recent studies based in an Irish setting in our literature search.

### European studies

A study performed in Austria looked at diagnoses over two one year time periods (2003-04 N = 1,474, and 2004-05, N = 1,833).<sup>7</sup> The authors noted significant decrease in depressive disorders (18.5% in the initial survey, 14.3% in the repeat survey) and significant increase in adjustment disorders (21.4% in the initial survey, 24.5% in the repeat survey), and suggested that the patients in the second survey may have had less severe psychiatric morbidity, and also suggested that increased awareness of psychiatric co-morbidity in the second survey, may have accounted for the increase in adjustment disorders.

A study in Germany by the same author looking at diagnoses over two individual time periods (1990, N = 713 and 1998, N = 1,025), in a liaison psychiatry consultation service, indicated that there were changes in patterns of diagnosis over time.<sup>2</sup> The authors noted there were significant increases in rates of diagnosis for delirium (put down to increasing recognition by the referring teams) and other psychoactive substance use disorders (increased from 2.7-5%).

### Liaison psychiatry groups studies

In some regions groups of liaison psychiatrists have combined to perform research in multiple consultation-liaison psychiatry services. The European Consultation-Liaison Workgroup (ECLW) collaborative study described consultation-liaison service delivery by 56 services from 11 European countries (N = 12,279), excluding patients presenting with deliberate self harm.<sup>1</sup>

Commonest diagnoses included mood disorders (18.7%), organic mental disorder (17.7%), substance abuse disorders (13.3%), and adjustment disorder (12.4%; figure includes PTSD diagnoses).

Another multi-centre investigation was performed by the Consultation-Liaison Group in Italy (N = 4,182) involving seventeen hospitals.<sup>8</sup> The authors noted differences between their results, and results published in other European countries, and suggested that this was likely in part determined by mental health organisation settings, and in part by the specific characteristics of the patients.

### US studies

A large study in the US looked at 4,429 consecutive referrals to a consultation liaison service, between the years of 1988-1997.<sup>9</sup> Interestingly the specific diagnosis of adjustment disorder was variable in this study with a rate of 29.8% in 1988, and 13.5% in 1997. Also notable from this study was the high rate of organic mental disorders (40.1%).

The age categories in this study were comparable to our own study, with patients aged 66-75 years totalling 14% (12% in our study), and patients aged over 75 years totalling 13.5% (11.4% in our study).

Reasons for the high rate of organic mental disorders are not fully clear, with one possibility being a higher rate of

Table 3 (i): Results from other studies reporting on diagnoses in liaison psychiatry consultation services

Diagnostic categories (%)	Ramchandani et al, 1997, DSM-IV	Gala et al, 1999, ICD-10	Rothenhauser et al, Survey A, 2001, DSM-III-R	Rothenhauser et al, Survey B, 2001, DSM-III-R	Huyse et al, 2001, ICD-10	Diefenbacher et al, 2002, DSM- III-R
Depressive disorders			9.4	9.3		
Bipolar Disorders			1.1	1.4		1.7
Depressive disorders and adjustment disorders with depressed mood						28.1
Mood disorders	10	19.4			18.7	
Alcohol related disorders			6.0	8.2		
Substance related disorders other than alcohol			2.7	5.0		
Substance related disorders including alcohol	10	6.3			13.3	8.5
Delirium			11.5	16.6		
Dementia/Cognitive disorder			2.5	2.6		
Organic mental disorders	24	10.7			17.7	40.1
Disorders secondary to medical conditions	4					
Psychotic disorders	16	5.6	3.1	4.6	4.4	4.7
Anxiety disorders		13.9	5.2	4.8		
Somatoform disorders		4.8	19.1	15.2	7.5 (includes dissociative disorders and neurasthenia)	
Factitious disorders			1.3	1.5		
Adjustment disorders		14.4	21.6	19.4	12.4 (includes PTSD)	
Personality disorders	18	5.4	6.0	4.0	3.8	
Eating disorders			2.2	1.0	3.8	
Postpartum psychosis			1.0	1.2		
Other psychiatric disorders	14	2.8	0.6	1.7	0.6	
No psychiatric diagnosis/ Diagnosis deferred		17	6.7	3.5	12.3	6.4 (no axis 1 diagnosis)

referral for delirium in the managed care system in which this study was based, however the authors did not comment on possible reasons.

A study performed in California in 2001, including 901 inpatient referrals,<sup>10</sup> showed relatively high rates of mood disorders (40.7%). Reasons for this are not obvious, but the paper does include comparisons with previously published studies, which showed that the figures for mood disorders from their study was significantly higher than four other studies, while it was significantly lower than just one other study.

In a smaller study by Ramchandani, the authors noted that diagnoses of personality disorders were recorded in the notes of only 4% of patients (present in 18%), and substance related disorders in only 2% of patients (present in 10%),

and further suggested that the participating psychiatrists may have been reluctant to give controversial diagnoses to patients.<sup>11</sup>

#### Australian studies

Research in Australia compared consultation referral reasons, with diagnoses made by the liaison psychiatry service, between two time periods, 1999-2001 (N = 333) and 2003-2006 (N = 796).<sup>12</sup>

There were some differences between diagnoses in the initial study period and the second study period, however the authors did not comment on possible reasons for this, nor did they comment on whether these differences were significant.

Table 3 (ii): Results from other studies reporting on diagnoses in liaison psychiatry consultation services

Diagnostic categories (%)	Bourgeois, et al, 2005, DSM-IV-TR	Rothenhausler et al, Survey A, 2008, ICD-10	Rothenhausler et al, Survey B, 2008, ICD-10	Devasagayam et al, Survey A, 2008, DSM-IV	Devasagayam et al, Survey B, 2008, DSM-IV	Current Study, 2009, DSM-IV
Depressive disorders		18.5	14.3	13	32	16.6
Bipolar disorders		1.4	1.4	2	6	5.1
Mood disorders	40.7					
Alcohol related disorders		8.2	7.1	4	6	19.7
Substance related disorders other than alcohol		3.9	4.1	8	4	6.6
Substance related disorders including alcohol	18.6					
Delirium	21.1	18.1	18.8	14	12	11.7
Dementia/ Cognitive disorder	7.7	5.6	5.0	6	4	1.7
Cognitive disorder NOS	3.2					
Psychotic disorders	11.1	3.3	3.9	7.5	14	7.7
Anxiety disorders	9.0	3.4	3.4	4	4	9.1
Somatoform disorders		2.0	2.7	4	1	2.9
PTSD		2.0	1.8			
Adjustment disorders	10.8	21.4	24.5	26	12	7.1
Personality disorders						5.4
Borderline personality disorder				15	5	
Eating disorders		0.5	0.4	3	1	1.4
Postpartum psychosis		0.1	0			
Other psychiatric disorders	7.5	3.6	3.7	7	2	
No psychiatric diagnosis/ Diagnosis deferred	1.3	8.0	8.8			7.4

The authors in this study also noted that the final diagnoses displayed some differences from the referral reasons, particularly in relation to adjustment disorder and personality disorder.

## Discussion

It is difficult to directly compare our study with these international studies due to differing criteria used for diagnostic purposes, and the possible variability in patient populations between different hospitals. When comparing with the international studies, the diagnoses which stand out as being different in our study are the high rate of alcohol related disorders, and the low rate of adjustment disorders, and these are discussed in further detail below.

The referral rate of 2.2% of admissions in our study was

higher than that found in some other studies (Huyse *et al*,<sup>1</sup> 1.4%; Gala *et al*,<sup>8</sup> 0.7%), but lower than that found in others (Bourgeois *et al*,<sup>10</sup> 4.2%).

This referral rate was much lower than that reported among neurology admissions (6%) by Fitzgerald *et al* in Cork University Hospital.<sup>4</sup> A total of 11.4% of patients in our study were given more than one psychiatric diagnosis, which is lower than some of the other studies reviewed (Gala *et al*,<sup>8</sup> 15%; Bourgeois *et al*,<sup>10</sup> 25%).

## Alcohol related disorders

The rate of alcohol related disorders in our study was relatively high (19.7%). It should be noted that St Vincent's University Hospital is a national referral centre for liver transplants, however this is unlikely to explain entirely the higher

rates of alcohol related disorder presentations. There have been concerns raised previously about the rate of alcohol consumption in Ireland, however we found no definite figures published for alcohol related disorders.

A eurobarometer report on attitudes towards alcohol published in 2007, suggested that Ireland had the highest rate of binge drinkers in the EU, with 34% of people in Ireland reporting having five or more drinks on average at one sitting, which was more than three times the EU average of 10%.<sup>13</sup>

The liaison psychiatry study performed in Cork over 25 years ago had a rate of 10% for alcohol dependence syndrome (the only alcohol related disorder reported in this study), and as mentioned earlier, the authors reported that this was relatively high compared to other liaison psychiatry studies available at the time. In the study of referrals by the neurology service to a liaison psychiatry service in Cork by Fitzgerald *et al*, there were also high rates of alcohol use disorders (20%).<sup>4</sup>

A survey performed in the neurology service in the Mater Misericordiae Hospital in 2002, found a high rate of alcohol-related neurological problems being referred to their service (9.5% overall, and 20% in the 40-60 year age group).<sup>14</sup>

Reasons for the high rate of alcohol referrals and diagnoses in our service could be due to higher rates of alcohol misuse in our hospital, however this should be interpreted with caution, as what we have measured in this study is merely a proportion of the referrals within our service. Further research in the community and other Irish institutions would help in clarifying this situation, however this finding reinforces the increasing need for awareness of alcohol misuse among the Irish population.

### Depressive disorders and adjustment disorders

Differences between referral reason and clinical diagnosis was noted in our study, particularly in relation to referrals with a query for depressive disorder, similar to research by Devasagayam.<sup>12</sup>

For example, these patients were sometimes diagnosed with adjustment disorders, alcohol/substance use disorders, or with personality disorders (as outlined in the results section). There were few referrals for adjustment disorders and personality disorders in our study when compared with the diagnoses, perhaps due to poor awareness of these conditions. It is also possible that medical doctors may not be confident diagnosing adjustment disorder or personality disorder, and hence may ask for an assessment of mood when referring instead.

Another finding from our study was that alcohol related disorders and substance related disorders other than alcohol, were sometimes not present as a referral reason, but were subsequently identified by the liaison psychiatry service, as can be seen from the higher rates of diagnosis for these disorders than referrals.

There was a relatively low percentage of diagnosis of adjustment disorders in our study (7.1%) when compared with other international studies, and reasons for this are not fully clear. The rate of depressive disorders in our study was not dissimilar to other studies (16.6%).

Large reductions in diagnosis of adjustment disorder over time were noted in two of the international studies discussed above (Diefenbacher *et al*,<sup>9</sup> where rates decreased from 29.8-13.5%; Devasagayam *et al*,<sup>12</sup> where

rates decreased from 26-12%).

In the study by Diefenbacher, depressive disorders and adjustment disorders with depressed mood were put together in a single category, however the authors reported that the rates of depressive disorders other than adjustment disorders doubled over the 10 year period (increased from 6.4% to 14.7%). The authors noted that along with other possible reasons, one reason for this may be that differentiating between these two disorders is not always clear cut.<sup>15</sup> It is possible that without the use of structured clinical interviews, subjective clinical decisions may cause overlap between the diagnoses of these two conditions (eg. diagnosing an adjustment disorder with depressed mood may overlap with diagnosis of mild depressive episode).

### Liaison psychiatry diagnostic criteria

There have been calls for better definition and classification of patients seen by liaison psychiatry consultation services for some time now,<sup>16</sup> and some efforts have been made at standardising diagnoses in medical patients. Use of standardised tools and international consensus in establishing diagnoses, may help future research in this area. The European Consultation Liaison Workgroup have looked at this,<sup>17</sup> and other efforts have included the creation of the Diagnostic Criteria for Psychosomatic Research (DCPR), by an international group of psychosomatic investigators. Research into the DCPR has shown that it may be a useful and reliable tool, with good inter-rater agreement, in assessing medical patients with psychological distress,<sup>18</sup> however it remains to be seen if such a tool could become widely utilised.

### Limitations

The differences identified in the international literature search could in part be due to differing health systems and special interests of different hospitals, however some of these studies were performed as part of multi-centre investigations,<sup>1,8</sup> and the studies still provide some valuable comparisons.

In the first six month period registrars were not aware that the diagnoses recorded would subsequently form part of a study, and the diary was reviewed retrospectively at the end of the six month period.

In the second six month period, the registrars were aware that this was a continuation of the study, however the data was still recorded in the consultation diary in the same way, and the diary was reviewed retrospectively at the end of the six month period.

The diagnoses were determined in the same way for the two periods, so this is unlikely to have had a major impact on diagnoses given. Diagnoses used were clinical diagnoses (given following clinical assessment by the liaison psychiatry team) based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM-IV-TR) with no standardised tool used, which may have reduced the accuracy of some diagnoses, and did not allow for measurement of inter-rater reliability. The sample size of our study is relatively small when compared with some of the other international studies discussed, however to the best of our knowledge, this is the largest study reporting on reasons for referral and diagnoses in an inpatient liaison psychiatry consultation service in Ireland to date.

Declaration of Interest: None.

**Acknowledgements**

The authors would like to thank all staff in St Vincent's University Hospital who assisted in performing this survey including library staff, Dr Michelle Hill, Dr Patricia Burke, and Dr Caroline Meagher.

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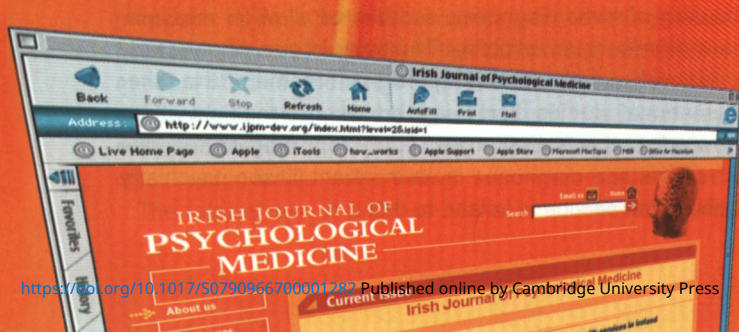
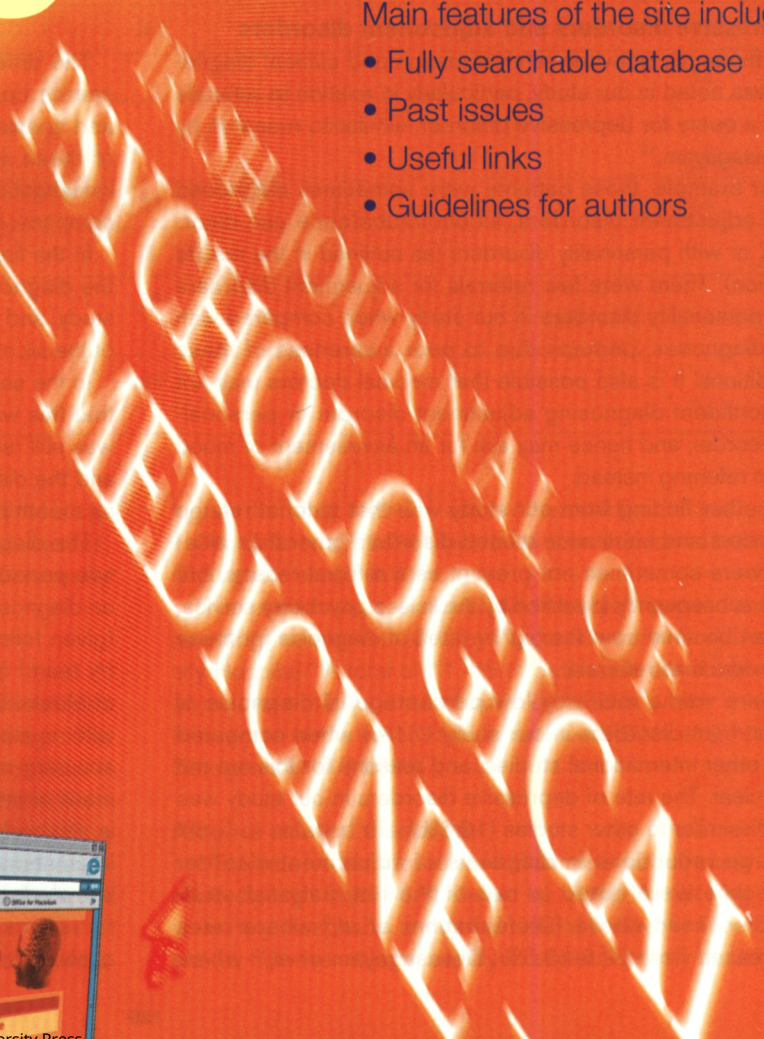
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# Communication is important<sup>1-3</sup>



## Ebixa

Approved from the moderate stage of Alzheimer's Disease onwards<sup>5</sup>

### Abbreviated Prescribing Information:

For full prescribing information refer to the Summary of Product Characteristics. **Name:** Ebixa **Active Substance:** Memantine Hydrochloride. **Indication:** Treatment of patients with moderate to severe Alzheimer's disease. **Dosage & Administration:** Treatment should be initiated and supervised by a physician experienced in the diagnosis and treatment of Alzheimer's dementia. Therapy should only be started if a caregiver is available who will regularly monitor the intake of the medicinal product by the patient. Treatment is orally either as tablets (10 mg) or solution (10 mg/g) taken with or without food at the same time every day. The solution should only be dosed onto a spoon or into a glass of water using the pump. Maintenance dose is 20mg/day (two tablets or 2ml solution [4 downward strokes] once daily). Treatment starts with 5mg/day (half a tablet or 0.5 ml solution [1 downward stroke] once daily) for the first week; the 2nd week 10mg/day (one tablet or 1 ml solution [2 downward strokes] once daily); the 3rd week 15mg/day (one and a half tablets or 1.5ml solution [3 downward strokes] once daily) and the 4th week 20mg/day (two tablets or 2ml solution [4 downward strokes] once daily). Moderate renal impairment 10mg/day (one tablet or 1 ml solution [2 downward strokes] once daily), if well tolerated after 7 days the dose can be titrated up to 20mg/day (two tablets or 2 ml solution [4 downward strokes] once daily). Severe renal impairment- dose is 10 mg/day (one tablet or 1 ml solution [2 downward strokes] once daily). Mild-moderate hepatic impairment- no dose adjustment. Severe hepatic impairment- no data available. Children & Adolescents: Not recommended. **Contraindications:** Hypersensitivity to the active substance or any of the excipients. **Pregnancy and Lactation:** **Pregnancy:** Memantine should not be used in pregnant women unless clearly necessary. **Lactation:** Memantine should not be used in women who are breastfeeding. **Special Warnings and Precautions for use:** Caution is recommended in patients with epilepsy. Caution is advised in patients with raised urine pH as this may elevate plasma levels. Clinical trial data are limited on patients with recent myocardial infarction, uncompensated congestive heart failure and uncontrolled hypertension and patients with these conditions should be closely supervised. Avoid concomitant use of NMDA antagonists (see also interactions). Patients with sugar intolerance should not take Ebixa. Patients should be warned to take special care if driving and using machines as Ebixa has minor to moderate influence on these tasks. **Interactions:** Effects of L-Dopa, dopaminergic agonists and anticholinergics may be enhanced. Effects of barbiturates and neuroleptics may be reduced. Concomitant administration of Ebixa with antispasmodic agents e.g. dantrolene and baclofen

can modify their effects, dose adjustments may be necessary. Plasma levels of cimetidine, ranitidine, procainamide, quinidine, quinoline and nicotine may be increased. Co-administration with hydrochlorothiazide (HCT) may lead to a reduced serum level of HCT. Concomitant use of NMDA antagonist- amantadine, ketamine, dextromethorphan or phenytoin should be avoided. Close monitoring of prothrombin time or INR is advisable for patients treated concomitantly with oral anticoagulants. **Adverse reactions:** Common ( $\geq 1/100$  to  $< 1/10$ ) headache, somnolence, hypertension, constipation, dizziness, dyspnoea and drug hypersensitivity. Uncommon reactions ( $\geq 1/1000$  to  $< 1/100$ ): cardiac failure, fatigue, fungal infections, confusion, hallucinations (mainly in severe Alzheimer's disease), venous thrombosis/thromboembolism, vomiting, gait abnormal. Very rare ( $< 1/10,000$ ): seizures. Not known: Isolated cases of pancreatitis and psychotic reactions have been reported post-marketing. Alzheimer's disease has been associated with depression, suicidal ideation and suicide. In post-marketing experience these events have been reported in patients treated with memantine. **Overdose:** Symptomatic treatment. **Elimination:** Mainly in unchanged form via the kidneys. **Legal Category:** POM. **Marketing Authorisation Holder:** H.Lundbeck A/S, 9 Otttilavej, DK-2500 Valby, Denmark. **Marketing Authorisation Numbers:** EU/1/02/219/005 Ebixa 10mg/g Oral drops solution-50g bottle, EU/1/02/219/006 Ebixa 10mg/g Oral drops solution-100g bottle, EU/1/02/219/007 Ebixa Tablets 10mg, 28 pack size, EU/1/02/219/008 Ebixa Tablets 10mg, 56 pack size. Further information may be obtained from: Lundbeck (Ireland) Ltd., 7 Riverwalk, Citywest Business Campus, Citywest, Dublin 24.

**Date of Preparation:** June 2010

**References:** 1. Ferris et al. 2009. *Alzheimer's & Dementia* 5;369-374. 2. Emre et al. 2008. *Journal of Alzheimer's Disease* 14;195-199. 3. Hofbauer et al. 2009. Presented at the 12th Intl. Conference on *Alzheimer's Disease*, July 11-16. 4. Claxton et al. 2001. *Clinical Therapeutics*, 23;1296-1310. 5. Ebixa Summary of Product Characteristics.

Some studies include patients stable on acetylcholinesterase inhibitors.

1EB/09/10



20 mg Once-Daily  
**Ebixa**  
memantine