

Bipolar disorder

Data Focussed Commentary

Assessment, diagnosis and initiation and modification of bipolar disorder treatment is routinely carried out by specialists in mental health. GPs and other primary health care professionals have an important role in recognition and referral, and for regular review of physical, mental and social well-being of patients with this life-long serious mental health disorder.

As recognised in the NICE guideline for bipolar disorder,¹ there is considerable “off-label” prescribing of drugs in bipolar disorder. However, prescribers should not be deterred from prescribing drugs off-label provided there is good evidence (e.g. NICE guidance) for this. The only drugs licensed for bipolar disorder are shown in Table 1.²

Table 1. Drugs licensed for bipolar disorder (as of September 2008)

Drug	Indication in bipolar disorder
Lithium	Treatment and prophylaxis
Olanzapine	Moderate to severe manic episode, and prevention of recurrence in patients who responded to olanzapine previously
Quetiapine	Manic episodes
Aripiprazole	Moderate to severe manic episodes and for the prevention of recurrence in patients who responded to aripiprazole previously
Risperidone	Mania
Valproate (Depakote)	Acute manic episodes
Carbamazepine	Prophylaxis of manic-depressive psychosis in patients unresponsive to lithium therapy
Lamotrigine	<i>Not licensed</i> in the UK for bipolar disorder

As well as their role in the management of acute episodes, NICE recommends that lithium, olanzapine or valproate should be considered for long-term treatment of bipolar disorder, but valproate should not be prescribed routinely for women of child-bearing potential.¹ Other drugs that are second line or add-on options include lamotrigine, carbamazepine, other antipsychotics, including risperidone, quetiapine, aripiprazole, and antidepressants (usually SSRIs). Aripiprazole was not licensed for bipolar disorder when NICE was considering its guidance. NICE recommends that antidepressants should not be used long-term routinely.

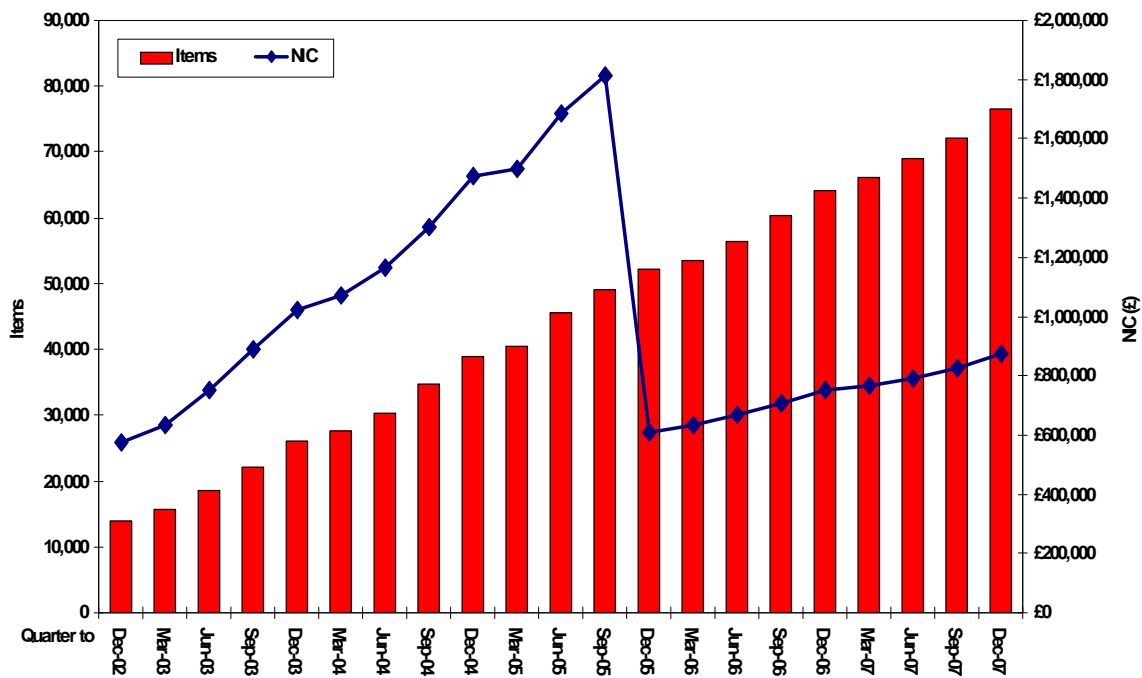
Although lithium is used mainly for the treatment of bipolar disorder, other drugs (anticonvulsants, antipsychotics or antidepressants) are mainly used in other indications. There is one form of valproate semisodium (Depakote) licensed for the management of bipolar disorder in the UK, however, sodium valproate (generic available) has been used widely off-label, and is less expensive. Only in the case of lithium therefore, can prescribing trends be reliably taken to relate to its prescribing patterns in bipolar disorder. Although data are available for valproate semisodium, it is not known what proportion of its prescribing relates from switches from off-label prescribing of sodium valproate.

Prescribing and monitoring trends for lithium and valproate semisodium

In September 2007, NICE published an implementation report for the use of valproate.³ In the 12 months to March 2007, 798,000 prescriptions for lithium were dispensed at a cost of £1.45 million. In the same period, 267,000 prescriptions for semisodium valproate were dispensed at a cost of £3,075, an increase of 22.37% on the previous 12 months. There were 2.03 million items for sodium valproate dispensed at a cost of £24.17 million, it is not known what proportion of this cost was off-label prescribing for bipolar disorder.

Figures 1 and 2 show the trends in prescribing volumes and costs for lithium and semisodium valproate (Depakote) up to December 2007.

Figure 1. Trends in prescribing of and spending on lithium in general practice in England

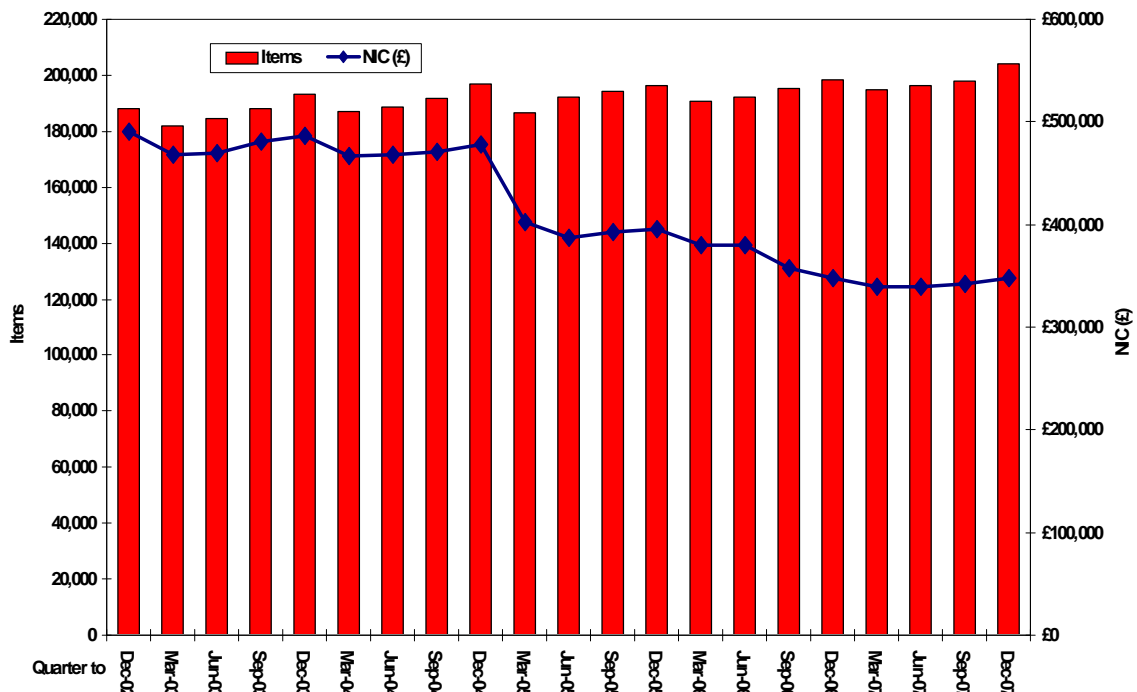


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Figure 2. Trends in prescribing of and spending on valproic acid (Depakote®) in general practice in England

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Lithium

It can be seen in Figure 1 that there is a slight but gradual upward trend in lithium prescribing up until the last quarter of 2004. In 2005 and 2006 the use of lithium in the community evened out. The prescribing rate is around 200,000 prescriptions per quarter, as at September to December 2007.

Monitoring of lithium levels is part of the mental health domain of the Quality and Outcomes Framework (QOF). The information collected from this area of the QOF give a useful indication of the extent to which lithium levels are being monitored in primary health care. The overall scores for England suggest an overall improvement in lithium monitoring, as recorded in general practice, since the QOF was introduced in April 2004. The overall achievement score for each indicator is given in Table 2.

Table 2. Quality and Outcomes Framework % achievement for lithium monitoring indicators, England.³

QOF indicator	QOF period		
	2004-05	2005-06	2006-07
MH 3. The percentage of patients on lithium therapy with a record of lithium levels checked within the previous 6 months.	90.9%	95.5%	n/a
MH 4. The percentage of patients on lithium therapy with a record of serum creatinine and TSH in the preceding 15 months.	91.1%	95.9%	96.8%
MH 5. The percentage of patients on lithium therapy with a record of lithium levels in the therapeutic range within the previous six months.	74.4%	90.0%	90.5%

Valproate

The numbers of prescriptions for valproate semisodium has increased each quarter since its introduction. The sharp drop in cost shown in Figure 2, is because the price of Depakote was substantially reduced in 2005 under the pharmaceutical price regulation scheme. A key factor in the choice of valproate amongst prescribers has been drug cost, although the difference between the prices of the two forms of valproate (semisodium valproate and sodium valproate) is not now as great as it was (Table 3).

Table 3. Net ingredient cost of forms of valproate (1000mg/day) (Drug Tariff September 2008)

Form of valproate	Drug costs (£ NIC)
Semisodium valproate (Depakote)	1000mg/day = £0.54
Sodium valproate (generic)	1000mg/day = £0.44

One of the priorities for implementation in the NICE guideline is the recommendation that prescribers should not routinely prescribe valproate for women of childbearing potential.¹ The NICE cost impact report for implementing the bipolar disorder guideline in England expected a reduction in the proportion of women of childbearing potential with bipolar disorder routinely prescribed valproate.

NICE implementation recommendations

NICE has published advice on implementation of bipolar disorder.⁴ This contains suggestions for improving communications, between primary and secondary care, raising awareness of referral criteria and NICE recommendations for pharmacological management and medication review, the effect of bipolar disorder and its treatment on conception, and concerns in pregnancy. Enabling access to specialist advice and services, especially in times of crisis, and the provision of individualised care plans, are key components of management.

Key aspects for implementing the NICE guideline include recognition and diagnosis for children and adolescents, pharmacological management for women of child-bearing potential, long-term pharmacological management and support to patients who have gained weight during pharmacological treatment, and an annual review of physical health.

NICE makes a number of recommendations about the pharmacological management of people with bipolar disorder, which need to be communicated effectively to prescribers and those who advise them, both in primary and in secondary care. Emphasis should be put on the circumstances for initiating and managing long-term pharmacological treatment and the considerations for deciding on the agent of choice, using protocols and formularies as appropriate.⁴

NICE recommends that people with bipolar disorder should have an annual review of their physical health. It will be important to review local service provision and staffing to ensure that there are monitoring and early warning systems to identify who requires an annual review. It may be necessary to assess who takes responsibility for offering physical health checks locally. Key aspects to focus on include recognition and diagnosis for children and adolescents, pharmacological management for women of child-bearing potential, long-term pharmacological management and support to patients who have gained weight during pharmacological treatment, and an annual review of physical health. Provision of dietary advice and access to specialist dietary support is important, especially for those prescribed olanzapine, which is particularly associated with weight gain.⁴

Some key questions

1. Are GPs familiar with the referral criteria both for patients with suspected bipolar, and for those patients with a conformed diagnosis who join the practice?
2. Are prescribers aware of NICE's recommendations for drug treatment for the long-term management of bipolar disorder?
3. Do formularies or policies relating to the treatment of bipolar disorder need to be modified to be consistent with NICE guidance?
4. Are there any women of child-bearing potential receiving valproate, and are reasons for exceptional prescribing justified in the notes?
5. Do those patients diagnosed with bipolar disorder have a comprehensive and integrated care plan, which covers both primary and secondary care aspects?
6. Are the health professionals who the patient (or their carer/family) should contact in times of crisis clearly identified?
7. Do all patients with bipolar disorder receive a yearly check up of physical health, including monitoring of the weight, blood glucose, blood lipids (if >40 years), and blood pressure?
8. Are other specific monitoring tests, including serum levels for lithium, valproate and carbamazepine, being carried out routinely in accordance with NICE guideline recommendations?
9. Are there systems in place for dietary advice and specialist support for those receiving antimanic medications?

10. Are patients receiving olanzapine being monitored at least every three months for weight and height (and after one months following initiation)?
11. Are anti-manic medications being prescribed for prophylaxis for sufficient time (at least 6 months) to establish their effectiveness?
12. Are there patients with bipolar disorder who are being treated with antidepressants long-term, and if so, is this justified and the reason recorded in the notes? Are these people also prescribed anti-manic drugs, as recommended?
13. Are those people who would benefit from psychological therapy able to obtain therapy in a timely manner and of sufficient intensity (at least 16 sessions should be offered over 6 to 9 months)?

References:

1. National Institute for Health and Clinical Excellence. Bipolar disorder. The management of bipolar disorder in adults, children and adolescents, in primary and secondary care. Clinical Guideline 38. July 2006. Accessed from <http://guidance.nice.org.uk/cg38>
2. Summaries of Product Characteristics. Accessed from www.medicines.org.uk
3. NICE implementation uptake report: lithium and valproate prescribing for bipolar disorder. December 2007. Accessed from www.nice.org.uk/media/5DF/4C/NICEImplUptakeReportLithiumValproate.pdf
4. NICE implementation advice. Bipolar disorder. Accessed from: www.nice.org.uk/guidance/index.jsp?action=download&o=30199