Modafinil: Restrictions on indications and evidence for off-label uses

Over £2.7 million is spent annually on modafinil in England (ePACT Feb to April 2015). QIPP projects in this area focus on reducing modafinil prescribing for safety reasons.

Background

Modafinil is an oral 'wakefulness-promoting' agent acting on the central nervous system.[1] Its precise mode of action is unknown, but involvement of dopamine and norepinephrine is most likely.[2,3] Post-marketing data has revealed that modafinil can cause serious adverse effects including psychiatric disorders, cardiovascular symptoms and serious skin and multi-organ hypersensitivity reactions. A review by the European Medicines Agency (EMA) in January 2011, has led to restrictions on indications.[3]

Recommendations

- Limit prescribing of modafinil to the treatment of narcolepsy (the only licensed indication in the UK),[1] due to lack of evidence on safety and efficacy in other (off-label) conditions. Only prescribe modafinil in patients where a diagnosis of narcolepsy has been made by a specialist in accordance with diagnostic criteria. Ensure prescribing is for generic modafinil. Prescribing according to an agreed shared care guideline (SCG) is advised - see separate PrescQIPP SCG template on the link above.
- Monitor all patients prescribed modafinil for the potential risk of serious adverse drug reactions (ADRs), which include cardiovascular (CV) symptoms (hypertension and irregular heartbeat), psychiatric disorders (suicidal-ideation, mania and hallucinations), skin and multi-organ hypersensitivity reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis).[2]
- Review modafinil in off-label conditions to reduce inappropriate prescribing where there is insufficient evidence of efficacy and safety such as:
  - Fatigue in Multiple Sclerosis (MS), Parkinson's disease (PD), depression, post-stroke and lung cancer
  - Apathy in Alzheimer's disease
  - Adjunct in schizophrenia
  - Attention Deficit Hyperactivity Disorder (ADHD)
  - Misuse (cognitive enhancement)
  - Chronic fatigue syndrome.
- GMC good practice in prescribing states that doctors should be satisfied there is sufficient evidence or experience of using the medicine to demonstrate its safety and efficacy, also taking responsibility for prescribing an unlicensed medicine and overseeing the patient's care, monitoring and any follow-up treatment.[4]
- Manage fatigue in MS by assessing and offering treatment for anxiety, depression, difficulty in sleeping and any potential medical problems such as anaemia or thyroid disease. Consider mindfulness-based training, CBT or fatigue management. Advise people that aerobic, balance and stretching exercises including yoga may be helpful.[5]
- Check for reversible causes of fatigue in PD such as depression, poor sleep hygiene and drugs associated with altered sleep pattern.[6] For sleep disturbance at night, review all medications and avoid (where possible) any drugs that may affect sleep or alertness, or may interact with other medication (e.g. selegiline, antihistamines, H_2 antagonists, antipsychotics and sedatives).[7]

Supporting evidence

The EMA concluded that risks outweighed benefits in clinical trials for all indications other than narcolepsy, so these were withdrawn from marketing authorisations.[8] Prescribers should be aware of modafinil's safety profile and monitor patients appropriately.[3]

In 2013 NICE published ESUOM9: Fatigue in multiple sclerosis: modafinil. This concluded that two small placebo-controlled randomised controlled trials (RCTs) did not find any statistically significant evidence that modafinil improved fatigue in adults with MS (of any disease pattern). The RCTs did not provide any evidence of longer-term safety and efficacy of modafinil for treating fatigue in MS.[9]

There is insufficient evidence in efficacy and safety for all off-label use.

Savings

Reducing modafinil prescribing by 50% would save more than £1.3 million over 12 months.

This equates to £2,408 per 100,000 patients.

References

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http://www.prescqipp.info/resources/viewcategory/383-modafinil

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