CASE AUTH/2704/3/14

MEDICINES MANAGEMENT PHARMACIST v FLYNN PHARMA

Circadin journal advertisement

A medicines management pharmacist referred to a claim in a Flynn Pharma Ltd advertisement in Prescriber for Circadin (melatonin) that 'Current guidance states that, when a hypnotic is indicated in patients aged 55 and over, prolonged-release melatonin should be tried first'. The claim was referenced to Wilson *et al* (2010) which the complainant stated was the 'British Association for Psychopharmacology [BAP] consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders'. The complainant alleged that this was hardly current guidance and was misleading as he/she was sure most others would take 'current guidance' to mean that recommended by the National Institute for Health and Care Excellence (NICE) or the All Wales Medicines Strategy Group (AWMSG) in Wales.

The detailed response from Flynn Pharma is given below.

The Panel noted that the complainant stated he/she interpreted the claim to mean guidance recommended by NICE or AWMSG in Wales. The Panel queried how many readers would similarly interpret the claim as such.

The Panel noted that Wilson *et al* was a consensus statement written by eighteen members of BAP. The Panel was unsure of the criteria used to select the authors and noted that guidance from a nationally recognised body was different from that issued by a small consensus group of eighteen members. However, the abstract referred to the document as the 'The British Association for Psychopharmacology guidelines'. The process for agreeing the final document was described in the abstract which stated 'All comments were incorporated as far as possible in the final document which represents the view of all participants although the authors take final responsibility for the document'. BAP published the Journal of Psychopharmacology in which the guidelines appeared. The advertisement at issue included a reference but this did not refer to BAP; only the publication details were cited.

The Panel noted Flynn Pharma's submission that it had played no part whatsoever in the process by which BAP selected the therapy area (insomnia), or formulated its consensus statement and guidelines. The Panel further noted that Flynn Pharma had taken over marketing responsibility for Circadin from Lundbeck in January 2012. The BAP guidelines were published in 2010 following a consensus meeting in May 2009. The Panel noted that although Flynn Pharma had no relationship with BAP, Lundbeck was one of two companies which provided unrestricted grants to partially offset the costs of the BAP consensus statement meeting. The 'method' section of the document explained that observers from the companies were invited to attend but did not participate in the summary proceedings or in drafting the guidelines. The funding arrangements were described on the final page which included 'The costs of the meeting were partly defrayed by unrestricted educational grants from two pharmaceutical companies (Lundbeck and …)'. The Panel further noted Flynn Pharma's submission that one of the authors was a lead investigator in the clinical development of Circadin.

The Panel considered that the claim at issue 'Current guidance states…' was not sufficiently clear that the recommendation came from the 'British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders' nor did it reflect the status of that document and the role of the marketing authorization holder at the time the document was produced. The use of the term 'current guidance' in this context gave insufficient information about the nature and status of the guidance such that the claim at issue was ambiguous and therefore misleading. The Panel considered that on the information provided in the advertisement it was likely that readers would assume that the guidance had been issued by a nationally recognized body such as NICE or AWMSG. That was not so. The Panel ruled a breach of the Code.

A medicines management pharmacist complained about an advertisement (ref Circ/ADV/13/0483) for Circadin (melatonin) placed in Prescriber, Vol 25 issue 1/2 January 2014, by Flynn Pharma Ltd.

Circadin was indicated as monotherapy for the short-term treatment of primary insomnia characterised by poor quality of sleep in patients aged 55 or over.

COMPLAINT

The complainant referred to a claim in the advertisement that 'Current guidance states that, when a hypnotic is indicated in patients aged 55 and over, prolonged-release melatonin should be tried first'. The claim was referenced to Wilson *et al* (2010).

The complainant alleged that this was misleading as he/she was sure most others would take 'current guidance' to mean that recommended by the National Institute for Health and Care Excellence (NICE) or the All Wales Medicines Strategy Group (AWMSG) in Wales. The complainant stated

that on further investigation, he/she found that the reference was to the 'British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders'. The complainant alleged that this was hardly current guidance.

Flynn Pharma was asked to respond in relation to Clause 7.2 of the Code.

RESPONSE

Flynn Pharma submitted that the British Association for Psychopharmacology (BAP) guidelines remained 'current' in so far as they had not been revised or superseded by any other authoritative guidance in the management of insomnia. Wilson *et al*, published the BAP consensus statement on evidence-based treatment for insomnia, parasomnias and circadian rhythm disorders in 2010 which provided comprehensive statements to guide clinicians managing patients in primary or secondary care. BAP was an authoritative and long-standing professional group in the UK with a track record of producing guidance in a number of areas of psychopharmacology. A transparent and robust process in developing guidelines, and in dealing with industry relationships, sponsorship and declarations of conflicts of interest was followed. Flynn Pharma submitted that the authors were convened to review the literature and identify the standards of evidence in their area, with an emphasis on meta-analyses, systematic reviews and randomised clinical trials, where available. The group developed consensus statements and guidance based on the evidence base available. The section 'Treatment of insomnia in the elderly' recommended 'when a hypnotic is indicated in patients over 55, prolonged-release melatonin should be tried first'. This was entirely consistent with the claim in question and the guidance remained current.

Flynn Pharma submitted that more recent published statements and advice reinforced the validity of the claim at issue. For example the British National Formulary (BNF) 66th Edition (September 2013), Section 4.1.1 Hypnotics, stated:

> 'Elderly. Benzodiazepines and the Z-drugs should be avoided in the elderly because the elderly are at greater risk of becoming ataxic and confused leading to falls and injury'.

Flynn Pharma submitted that this reinforced and strengthened prescriber advice in an important and more vulnerable patient population. Previous editions of the BNF included the following non-specific advice:

> 'Elderly. Hypnotics should be avoided in the elderly because the elderly are at a greater risk of becoming ataxic and confused leading to falls and injury'.

Importantly, in stipulating which hypnotics should be avoided in the elderly, the updated BNF, clarified to prescribers that this cautionary statement did not apply to prolonged-release melatonin (Circadin).

In October 2013, the Midlands Therapeutic Review and Advisory Committee (MTRAC) published commissioning support advice to primary care, on the use of Circadin, replacing a previous and negative recommendation from 2009. The new and current recommendation was positive ie melatonin was suitable for prescribing in primary care for the treatment of patients over the age of 55 with a diagnosis of primary insomnia, and for up to 13 weeks. The updated MTRAC advice was based on a comprehensive review which included BAP 2010 and a number of published papers not available to the BAP group at that time. This was a category A recommendation. This review supplanted the previous (January 2009), which was negative and based on a more limited evidence base. The remit of MTRAC was to review selected pharmaceutical products to assess their clinical value, safety and suitability for use in primary care, and to support appropriate prescribing and commissioning. Guidance issued by MTRAC reflected the appropriateness of prescribing these products in the primary care setting, based on the best evidence available.

The approval of prolonged-release melatonin tablets 2mg, in June 2007, post-dated the last NICE technology appraisal in this therapy area (TA77, April 2004, Guidance on the use of zaleplon, zolpidem and zopiclone for the short-term management of insomnia). Whilst NICE often operated on a five year period before reviewing and updating its advice, Flynn Pharma understood that the NICE guidance was currently on a 'static' list.

More recently, NICE issued Good Practice Guidelines 2012 (Developing and updating local formularies), NICE recommended that for medicines that had not yet been considered, (or had not received a positive recommendation), for use in the NHS through a NICE technology appraisal, that NHS organisations should use other sources of high-quality information when appraising a medicine. MTRAC and BNF were specifically cited by NICE as relevant sources. Both were more recent sources and entirely consistent with, and in accordance with, the BAP 2010 guidelines.

Flynn Pharma submitted that it played no part whatsoever in the process by which BAP selected the therapy area (insomnia), or formulated its consensus statement and guidelines. BAP published its advice in 2010 following a consensus meeting in May 2009. Flynn Pharma only assumed marketing responsibility for Circadin in January 2012, taking over this responsibility from Lundbeck, which was one of two companies which provided unrestricted grants to partially offset the costs of the BAP consensus statement meeting. Clearly Lundbeck had an interest in the therapy area at the time but Flynn Pharma did not consider that the BAP guidelines were compromised in any way on that basis.

Flynn Pharma submitted that it did not have any relationship with any of the guideline authors. Since assuming responsibility for Circadin in 2012, Flynn Pharma had made declared payments to two of the authors who had delivered sponsored presentations

on Flynn Pharma's behalf. One was a lead investigator in the clinical development of Circadin and the other was a recognised international expert in the management of sleep disorders. Flynn Pharma had no and had never had any business relationship with Lundbeck.

In conclusion, Flynn Pharma stated that BAP 2010 guidance continued to be valid today and was further supported by more recent advice from BNF and MTRAC. There was not and nor was there anticipated to be any relevant guidance from NICE. In Wales, AWMSG had not, and would not consider Circadin since the resource impact of the product lay outside its role and remit (ie it was covered by AWMSG exclusion criteria). Flynn Pharma submitted that in its view the advertisement was fully compliant with the Code and specifically complied with Clause 7.2.

PANEL RULING

The Panel noted the clause cited by the case preparation manager, Clause 7.2. The 2014 Code came into operation on 1 January 2014 with a transition period for newly introduced requirements. Clause 7.2 was the same in the 2014 and 2012 Second Edition (amended) Codes, thus the Panel used the 2014 Code.

The Panel noted that the complainant stated he/she interpreted the claim 'Current guidance states that, when a hypnotic is indicated in patients aged 55 and over, prolonged-release melatonin should be tried first' to mean guidance recommended by NICE or AWMSG in Wales. The Panel queried how many readers would similarly interpret the claim as such.

The Panel noted that the claim was referenced to Wilson *et al* and it appeared that the claim was taken from the consensus statement written by eighteen members of the British Association for Psychopharmacology (BAP). The Panel was unsure of the criteria used to select the authors and noted that guidance from a nationally recognised body was different from that issued by a small consensus group of eighteen members. However, the abstract referred to the document as the 'The British Association for Psychopharmacology guidelines'. The process for agreeing the final document was described in the abstract which stated 'All comments were incorporated as far as possible in the final document which represents the view of all participants although the authors take final responsibility for the document'. BAP published the Journal of Psychopharmacology in which the guidelines appeared. The advertisement at issue included a reference but this did not refer to BAP; only the publication details were cited.

The Panel noted Flynn Pharma's submission that it had played no part whatsoever in the process by which BAP selected the therapy area (insomnia), or formulated its consensus statement and guidelines. The Panel further noted that Flynn Pharma had taken over marketing responsibility for Circadin from Lundbeck in January 2012. The BAP guidelines were published in 2010 following a consensus meeting in May 2009. The Panel noted that although Flynn Pharma had no relationship with BAP, Lundbeck was one of two companies which provided unrestricted grants to partially offset the costs of the BAP consensus statement meeting. The 'method' section of the document explained that observers from these companies were invited to attend but did not participate in the summary proceedings or in drafting the guidelines. The funding arrangements were described on the final page of the document which included 'The costs of the meeting were partly defrayed by unrestricted educational grants from two pharmaceutical companies (Lundbeck and ...)'. The Panel further noted Flynn Pharma's submission that one of the authors was a lead investigator in the clinical development of Circadin.

The Panel noted Flynn Pharma's submission regarding MTRAC guidance. This was used as reference to another claim in the advertisement at issue; 'Melatonin (Circadin) is suitable for prescribing in primary care'.

The Panel considered that the claim at issue in the advertisement 'Current guidance states...' was not sufficiently clear that the recommendation came from the 'British Association for Psychopharmacology consensus statement on evidence-based treatment of insomnia, parasomnias and circadian rhythm disorders' nor did it reflect the status of that document and the role of the marketing authorization holder at the time the document was produced. The use of the term 'current guidance' in this context gave insufficient information about the nature and status of the guidance such that the claim at issue was ambiguous and therefore misleading. The Panel considered that on the information provided in the advertisement it was likely that readers would assume that the guidance had been issued by a nationally recognized body such as NICE or AWMSG. That was not so. The Panel ruled a breach of Clause 7.2.

Complaint received **14 March 2014**

Case completed **30 April 2014**