ACMD

Advisory Council on the Misuse of Drugs

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James Brokenshire MP
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27th July 2010

Dear Minister,

Re: Tapentadol advice

I am writing to provide you with the Advisory Council on the Misuse of Drugs' (ACMD) consideration of the compound Tapentadol (3-[(1*R*,2*R*)-3-(dimethylamino)-1-ethyl-2-methylpropyl]phenol hydrochloride) (trade name Nucynta). Tapentadol is a painkiller that is likely to be marketed in the UK in the near future by a pharmaceutical company. However, there is risk of misuse of this psychoactive substance and of diversion from legitimate sources. It is therefore important that the harms of the drug are considered in relation to the Misuse of Drugs Act 1971. The ACMD's advice is set out below.

Tapentadol is a recently developed centrally-acting analgesic (painkiller) with two modes of action, as an agonist at the μ-opioid receptor and as a norepinephrine reuptake inhibitor. It was developed by Grünenthal Ltd in conjunction with Johnson & Johnson Pharmaceutical Research and Development.

The ACMD has received a presentation from Grünenthal Ltd [the company intending to market the substance]. The ACMD considered the nonclinical assessments (*in vitro* and *in vivo* assessments, intracerebral microdialysis and animal abuse related studies) and clinical assessments (human abuse liability assessment trial, other relevant clinical data drug dependence, drug withdrawal and tolerance) that have been carried out. After consideration of

the evidence of harms the ACMD conclude that the potential for abuse of Tapentadol is similar to that of other μ-opioid analgesics, including Hydromorphone and Morphine, (both controlled under Class A under the Misuse of Drugs Act 1971). Tapentadol presents a risk of addiction, potential illegal diversion and medicinal misuse.

On 22 June 2009, the Drug Enforcement Agency (DEA) in the United States approved the proposal to make Tapentadol a schedule II drug under the Controlled Substance Act. Further, on 23 June 2009, after having received approval from the FDA (Food and Drug Administration) and DEA, Tapentadol (immediate-relaese tablets) became available for prescription in the US for relief of moderate to severe acute pain in adults 18 years of age or older.

The Expert Committee on Narcotics Drugs in Germany also considered Tapentadol in terms of its abuse potential and considers that Tapentadol should be listed as a narcotic substance in schedule III ("Anlage III") of the German Law Narcotic Drugs (in the same category as Hydromorphone and Morphine). The control of Tapentadol in Germany came into force 23 December 2009.

The ACMD concludes that the abuse liability of Tapentadol would be substantial and has the potential to cause social harm through diversion and addiction. The ACMD, following its consideration of Tapentadol, recommends that Tapentadol should be controlled under the Misuse of Drugs Act 1971 in Class A – and Schedule II of the Misuse of Drugs Regulations 2001.

Yours sincerely,

Professor Les Iversen FRS