# ANONYMOUS v PROSTRAKAN

## Promotion of Abstral

**An anonymous physician alleged that an un-named ProStrakan representative had misled him/her with regard to the titration schedule for Abstral (fentanyl citrate). Abstral was indicated for the management of breakthrough cancer pain (BTcP) in adults using opioids for chronic cancer pain.**

**The complainant stated that he/she had been shown a document which looked like a prescription record card, but had not been given a copy of it. The complainant stated that the dosing looked simple. On day 1 the dose was 100mcg with a rescue dose of 100mcg. If pain relief was not obtained on day 1, the dose for day 2 should start at 200mcg with a rescue of 100mcg. This dose was used all day on day 2 and day 3 would start with a dose of 300mcg and so on until the right dose was reached.**

**The complainant stated that as he/she wanted to prescribe Abstral, he/she subsequently looked up the product information on-line and found that the information from the representative was totally different to the approved titration process. This sort of misinformation could affect patient care.**

**The detailed response from ProStrakan is given below.**

**The Panel noted that the complainant was anonymous and non-contactable and had provided little information and no documentation to support his/her complaint. As with any complaint, the complainant had the burden of proving his/her complaint on the balance of probabilities; the matter would be judged on the evidence provided by the parties.**

**The Panel noted from the Abstral summary of product characteristics (SPC) that all patients must start therapy with a single 100mcg sublingual tablet. If adequate analgesia was not obtained in 15-30 minutes a second 100mcg tablet could be given. If adequate analgesia was not obtained within 15-30 minutes of the first dose, an increase in dose to the next highest tablet strength should be considered for the next episode of BTcP. Dose escalation should continue in a stepwise manner until adequate analgesia was achieved. The maximum dose for the treatment of any episode of BTcP was 800mcg.**

**The Panel noted that ProStrakan had provided a copy of the Abstral Titration Chart which it assumed was the document referred to by the complainant. This chart showed that for the first episode of BTcP, patients should be given a 100mcg tablet with the option of a second tablet if the first was not effective after 15-30 minutes. If a second tablet had to be given then treatment of the second episode of BTcP should begin with a 200mcg tablet and the titration schedule continued in this stepwise manner until adequate analgesia or the maximum dose (800mcg) was achieved, whichever came sooner. The Panel noted the layout of the titration chart and queried whether the complainant had mistaken BTcP episodes 1 to 6 with treatment days 1 to 6. In the Panel's view the titration chart was in accordance with the titration schedule contained within the Abstral SPC.**

**The Panel noted that in training slides 'Abstral:product profile and clinical value' a slide headed 'Titration of Abstral' correctly referred to doses being increased, if necessary, with subsequent episodes of BTcP. Similarly a titration wheel showed that if a rescue dose had been required then the dose of the first tablet should be increased for the next episode of pain.**

**ProStrakan had not found evidence that any of its staff knew anything about the daily titration schedule referred to by the complainant. All of the materials provided by ProStrakan referred to the dose of Abstral being increased, if necessary, with subsequent episodes of BTcP in accordance with the SPC. On the basis of the information before it, the Panel considered that the complainant had not established, on the balance of probabilities, that a representative had advised him/her to titrate Abstral on a daily basis as alleged. No breach of the Code was ruled.**

An anonymous, non-contactable, pain physician, who also managed palliative care patients, complained about what an un-named representative had told him/her about the titration of Abstral (fentanyl citrate). Abstral, marketed by ProStrakan UK Ltd, was indicated for the management of breakthrough pain in adult patients using opioid therapy for chronic cancer pain. The exchange between the complainant and the representative had taken place at a meeting.

**COMPLAINT**

The complainant stated that he/she had asked the representative about the titration process for Abstral which he/she had heard was difficult. The complainant stated that the representative showed him/her a document which had been developed by a palliative care team in Scotland in collaboration with ProStrakan. The document looked like a prescription record card similar to a cardex system.

The complainant stated that the dosing looked simple. The first dose was the lowest strength of 100mcg with the rescue dose also being 100mcg. This was to be used for all episodes of severe pain on day 1. If pain relief was not achieved on day 1,

the dose for day 2 should start at 200mcg with a rescue of 100mcg. This dose was then used all day on day 2. Day 3 would start at 300mcg with a rescue of another 100mcg and so on until the right dose was reached. The complainant stated that the representative would not give him/her the information to take away because he/she did not have copies to hand out. The complainant considered this looked simple to prescribe and use as he/she could change the prescription each morning depending on how the patient had responded the previous day.

The complainant stated that he/she wanted to try Abstral in his/her next patient. As the information had not been provided to take away the complainant looked up the product information online and saw that the approved titration process was much quicker and did not keep the dosing the same for a full day. The information from the representative was totally different to the approved titration process.

The complainant alleged that this sort of misinformation affected the care of patients and should not be allowed, and he/she would never trust what a representative told him/her again.

When writing to ProStrakan, the Authority asked it to respond in relation to Clauses 2, 3.2, 7.2, 7.4, 9.1, 15.2, and 15.9 of the Code.

**RESPONSE**

ProStrakan stated that it had conducted a full review of its material which referred to the titration of Abstral and whilst none had matched the complainant's description, the Abstral Titration Chart (ref M017/0476) was identified which, without further information or evidence provided by the complainant, ProStrakan assumed was the item in question.

ProStrakan submitted that the titration chart was produced to assist health professionals with the recommended prescribing of Abstral and the titration in hospitals. The titration schedule in the chart was consistent with the Abstral summary of product characteristics (SPC) and the item was certified before use. It was available for representatives to distribute to health professionals. A copy of the chart was provided.

ProStrakan stated that it took all complaints very seriously and in that regard it had interviewed relevant staff connected to the promotion of Abstral and it became clear that titration was a frequent topic discussed by representatives and health professionals. However, none of the interviewees described a titration schedule that differed from that in the Abstral SPC. At the conclusion of each discussion each interviewee was read the titration schedule detailed in the complaint; none of them had encountered, or knew of, such a titration schedule. Indeed, each interviewee noted the time and care taken to train the teams on the titration process. None of the managers interviewed were concerned about their team's understanding of the Abstral titration process and all asserted that it was an issue that they regularly monitored on field visits. No manager had ever observed a representative differing from the titration schedule detailed in the SPC. One commented that generally accepted best practice was to have the customer repeat back the titration schedule in order to ensure that they fully understood the process.

ProStrakan stated that there was no specific briefing document on the use of the Abstral Titration Chart. The Abstral initial training course covered the titration process in detail (copies of the relevant training slides were provided - Module Three: Abstral Product Profile and Clinical Value (ref M017/0456)). The titration process for Abstral was covered in detail on page seven of this slide deck and ProStrakan considered that this was fully consistent with the titration schedule detailed in the Abstral SPC.

ProStrakan also provided a copy of the Abstral Titration Wheel (ref M017/0527) which was a further aid to the appropriate and recommended use of Abstral. As with the titration chart it could be distributed to health professionals at meetings and was certified before use.

In conclusion, ProStrakan stated that its representatives were thoroughly trained on the Abstral titration schedule. Indeed, this was a key component of the recommended use of the product. This training informed the correct use of a selection of promotional materials that in themselves aided understanding of the titration process and supported health professionals in the appropriate use of Abstral. ProStrakan considered that the training materials met the requirements of the Code and thus denied a breach of Clause 15.9. ProStrakan also maintained that its representatives were well aware of these standards as demonstrated in the interviews conducted as part of its investigation into this complaint. ProStrakan denied a breach of Clause 15.2.

ProStrakan submitted that further to this, the materials produced in support of this assertion themselves complied with the Code with regards to accuracy and accordance with the marketing authorization for the product. The titration schedule detailed in the titration chart and the titration wheel reflected the Abstral SPC. ProStrakan did not consider that Clauses 3.2 or 7.2 had been breached.

ProStrakan stated that neither the interviews nor the material review identified claims that were not capable of substantiation. ProStrakan thus denied a breach of Clause 7.4.

ProStrakan considered that high standards had been upheld, and no breach of Clause 9.1 had occurred. As a consequence it also considered that a ruling of a breach of Clause 2 was not justified in this instance.

ProStrakan stated that without a formal identification of the material in question or any further detail about

the representative concerned, a full investigation into the complaint was not possible. Whilst ProStrakan respected the complainant's anonymity, it noted that an anonymous complaint limited the company's ability to investigate the allegations in detail and deprived the company of the standard reassurances provided to companies by the PMCPA that the complainant had been asked to declare any conflict of interest.

In response to a request for further information, ProStrakan submitted that without a name or location to work from it was difficult to exactly define the scope of the investigation. However, given that the complainant identified him/herself as a 'pain physician' and not a general practitioner, ProStrakan assumed that he/she worked in secondary care and so it focussed its interviews on the specialist care team (SCT) which was responsible for promoting Abstral in secondary care only.

ProStrakan stated that it would not have been possible to interview every member of the SCT before it submitted its response in the timeframe available, so it interviewed all of the regional business managers (RBMs) for the team and one of the two representatives in the SCT who covered Scotland; the other representative had only just been appointed when the complaint was made. The individual interviewed did not recognise the titration schedule detailed by the complainant and did not know of anywhere in Scotland that used such a system. This view was also reflected by the RBM who covered the North of England and Scotland.

ProStrakan submitted that in addition to the field force interviews, head office staff, including senior managers involved in the commercialisation of Abstral, were also involved in the investigation. Details of those interviewed were provided.

ProStrakan stated that palliative care physicians were a key customer group for Abstral, and so its representatives regularly worked with them to educate prescribers on the appropriate use and titration of the product. In 2008, when Abstral was launched in the UK, materials were developed in collaboration with a leading palliative care physician. These items had subsequently expired and been discontinued. More recent materials had been developed in collaboration with palliative care physicians, but these materials did not match the description provided by the complainant and did not explicitly relate to titration.

As a part of its commitment to the support of UK healthcare and healthcare providers, ProStrakan offered financial support through sponsorship, grants and donations to those who requested such. This support was offered in accordance with the Code and approved in accordance with ProStrakan's relevant standard operating procedure (SOP). Sponsorship, grant and donation records were checked for the last two years. ProStrakan's records showed that a proportion of this funding had been provided to palliative care teams. However, this funding had almost exclusively supported attendance at educational events. The records did not show a funding request for a project which had resulted in a document such as that described by the complainant. One funding request directly related to the titration of Abstral and had been submitted by a physician seeking financial support to design and print a titration tool to assist health professionals in using Abstral. The financial support for this project had been approved but the item was still in development and had not yet been released.

ProStrakan stated that it was not currently part of any joint working agreements with anyone working in palliative care.

**PANEL RULING**

The Panel noted that the anonymous complainant had not provided any details as to where he/she worked; no details were provided as to the identity of the representative alleged to have given the complainant misinformation. The complainant had referred to being shown a document which had been developed by a palliative care team in Scotland; the complainant had not been given a copy and no documents were provided by the complainant in support of his/her complaint. The complainant was non-contactable and thus it was not possible to request further information. The Panel noted that, as with any complaint, the complainant had the burden of proving his/her complaint on the balance of probabilities; the matter would be judged on the evidence provided by the parties.

The Panel noted from the SPC, that Abstral was indicated for the management of breakthrough cancer pain (BTcP) in adults using opioids for chronic cancer pain. All patients must start Abstral therapy with a single 100mcg sublingual tablet. If adequate analgesia was not obtained in 15-30 minutes a second 100mcg tablet could be given. If adequate analgesia was not obtained within 15-30 minutes of the first dose, an increase in dose to the next highest tablet strength should be considered for the next episode of BTcP. Dose escalation should continue in a stepwise manner until adequate analgesia was achieved. The dose strength for the supplemental (second) sublingual tablet should be increased from 100 to 200mcg at doses of 400mcg and higher. The maximum dose for the treatment of any episode of BTcP was 800mcg.

The Panel noted that ProStrakan had provided a copy of the Abstral Titration Chart which it assumed was the document referred to by the complainant although it had not been developed in collaboration with a Scottish palliative care team. This chart showed that for the first episode of BTcP, patients should be given a 100mcg tablet with the option of a second tablet if the first was not effective after 15-30 minutes. If a second tablet had to be given then treatment of the second episode of BTcP should begin with a 200mcg tablet with an option of an additional 100mcg tablet if the 200mcg tablet did not provide adequate analgesia within 15-30 minutes. Treatment of the third episode of BTcP should begin with a 300mcg tablet and the titration schedule

continued in this stepwise manner until adequate analgesia or the maximum dose (800mcg) was achieved, whichever came sooner. The Panel noted the layout of the titration chart and queried whether the complainant had mistaken BTcP episodes 1 to 6 with treatment days 1 to 6. In the Panel's view the titration chart was in accordance with the titration schedule contained within the Abstral SPC.

The Panel noted that in training slides 'Abstral:product profile and clinical value' a slide headed 'Titration of Abstral' correctly referred to doses being increased, if necessary, with subsequent episodes of BTcP. Similarly the titration wheel showed that if a rescue dose had been required then the dose of the first tablet should be increased for the next episode of pain.

The Panel noted that ProStrakan had not been able to find evidence that any of its staff knew anything about the daily titration schedule referred to by the complainant. All of the materials provided by ProStrakan referred to the dose of Abstral being increased, if necessary, with subsequent episodes of BTcP in accordance with the SPC. On the basis of the information before it, the Panel considered that the complainant had not established, on the balance of probabilities, that a representative had advised him/her to titrate Abstral on a daily basis as alleged. No breach of Clauses 2, 3.2, 7.2, 7.4, 9.1 15.2 and 15.9 was ruled.

**Complaint received** **7 June 2012**

**Case completed** **2 July 2012**

# ANONYMOUS EMPLOYEE v GRÜNENTHAL

## Promotional mailings

**An employee of Grünenthal complained anonymously about the frequency and volume of Palexia (tapentadol) promotional mailings sent to health professionals and alleged that target customers would be sent a mailing after every call. The complainant noted that the Code stated that 'Restraint must be exercised on the frequency of distribution and on the volume of promotional material distributed' and that 'No more than eight mailings for a particular medicine may be sent to a health professional in a year'. The complainant alleged that as Palexia mailings were sent to target customers after every call, in addition to other Palexia mailings, some customers could get more than eight mailings in a year and/or several mailings in a short space of time.**

**The detailed response from Grünenthal is given below.**

**The Panel noted that the supplementary information referred to by the complainant stated, *et al*, that in the first six months following the launch of a new medicine, a health professional could be sent up to four mailings about the medicine and that no more than eight mailings for a particular medicine might be sent to a health professional in a year.**

**The Panel noted that a marketing newsletter provided by the complainant implied that a Palexia brand reminder mailing would be sent to target GPs after every call. Grünenthal submitted that this was not so; the mailing would only be sent once, following the first contact with the customer in relation to Palexia from April 2012. This point could have been more clearly stated in the newsletter.**

**With regard to the volume of mailings the Panel noted that Grünenthal had provided information to show that between February 2011 and June 2012 no GP would have received more than four Palexia mailings and the maximum number received by any hospital health professional was two. The Panel considered that there was no evidence to show that any health professional had received more than eight mailings in a year as alleged. No breach of the Code was ruled.**

**With regard to the frequency of mailings the Panel noted that it was possible that some GPs might have received the MIMS Palexia announcement mailing (sent March 2012), the brand reminder mailing (sent from April 2012) and two mailings about a meeting (sent May-June 2012) in successive months. The Panel considered that in the circumstances this was not unacceptable. No breach of the Code was ruled.**

**The Panel consequently considered that with regard to the requirements for mailings there had not been a failure to maintain high standards. No breach of the Code was ruled.**

An anonymous, non-contactable employee of Grünenthal Ltd complained about the frequency and volume of Palexia (tapentadol) promotional mailings sent to health professionals.

**COMPLAINT**

The complainant alleged that after every call made on a target customer, Grünenthal sent that customer a Palexia 'brand reminder mailer' and dosage card. The complainant noted that Clause 11.2 of the Code stated that 'Restraint must be exercised on the frequency of distribution and on the volume of promotional material distributed' and also that 'No more than eight mailings for a particular medicine may be sent to a health professional in a year'. As mailings were sent after every call made on target customers, in addition to other promotional mailings for Palexia, some customers could get more than eight mailings in a year and/or several mailings in a short space of time.

The complainant provided a copy of a marketing newsletter which was sent to representatives in March. The newsletter stated that the brand reminder mailing would enhance the memorability of representatives' calls. The reader was informed that 'Your call on any IPTI customer with Palexia will be picked up in [the customer relationship management system], and then within 7 days we will mail the customer a letter and an additional dosage card reminding them of the call you made. This will start from the end of March.' The newsletter also referred to a second mailing programme which would also start in March, ie the MIMS product announcement on Palexia which would go to 10,000 UK specialists.

When writing to Grünenthal, the Authority asked it to respond in relation to Clauses 9.1 and 11.2 of the Code.

**RESPONSE**

Grünenthal explained that the Palexia brand reminder mailing (ref P12 0056a), referred to by the complainant was designed as a contact-activated mailer to selected GPs (maximum 4,500). The mailing consisted of a letter which reviewed the content of that contact and a dosage and titration leavepiece (ref P12 0056). The mailings were first sent out in April 2012 and this initiative would continue until December 2012. The process behind the mailing was automatic to ensure that it was only sent once to any GP during its eight month active period.