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***Targin*[®] (oral oxycodone/naloxone prolonged-release tablet) now launching across Europe to control severe chronic pain with significantly reduced risk of opioid-induced constipation**

First analgesic therapy to combine oxycodone, a strong opioid, with naloxone, an opioid antagonist, offers a new treatment option for physicians

Cambridge, 26 January 2009: Mundipharma today announced that 13 countries* to date have received approval of ***Targin***, a new combination therapy designed to control severe chronic pain whilst counteracting opioid-induced constipation, a common and often debilitating side effect associated with opioid treatment^{1,2,3}. A period of European launches will now be initiated.

Targin is an oral fixed combination of prolonged-release combination of oxycodone, a strong opioid agonist, and prolonged-release naloxone, an opioid antagonist. The Phase III clinical trial programme, which included 1,064 patients, demonstrated that ***Targin*** provides equivalent pain relief to prolonged-release oxycodone alone, whilst significantly reducing the risk of opioid-induced constipation.^{1,2,3} ***Targin*** has also been proven to provide pain relief that lasts for up to 12 hours from the first dose.^{1,2,3}

Although highly effective in the control of pain, the use of opioids is associated with opioid-induced bowel dysfunction. Its primary symptom is constipation,⁴ which can affect up to 95 percent of patients.⁵ Constipation can have a severe impact on patient quality of life⁶ and is one of the most common reasons patients avoid or discontinue pain therapy with strong opioids, compromising effective analgesia.⁷

One chronic pain patient from the UK, describing his experience, said: "When my pain got worse my doctor prescribed me a stronger painkiller. When I started taking it, although the pain got much better I started feeling really bloated and got terrible cramps in my stomach. It was so bad that I had to stop taking the medication, even though it was the only thing that gave me any relief."



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Opioid-induced constipation is often overlooked and inadequately managed.^{7,8,9} Whilst treatments such as laxatives can be used in conjunction with opioids to help alleviate its symptoms, they do not treat the cause of the problem⁶ and often do not provide adequate relief for patients¹⁰ and can cause other side effects.

“**Targin** is a significant development in the management of severe chronic pain,” comments Dr Gerhard Müller-Schwefe, President of the German Pain Association. “Clinicians treating pain must ensure we treat our patients not only with the most appropriate opioid to ensure adequate pain control, but also with a treatment which may minimise the incidence and impact of opioid-induced constipation, which can have a significant impact on patient quality of life.”

Opioid treatments provide pain relief by attaching to opioid receptors located in the brain and spinal cord to reduce the perception of pain. However, opioids also attach to peripheral opioid receptors in the gut, interfering with the ability of muscles to contract which slows gastrointestinal motility. They also influence secretion and increase the absorption of fluid in the gut, drying out gut contents and further impeding their passage through the digestive system, resulting in opioid-induced constipation.

Due to its very low bioavailability when given orally the naloxone component of **Targin** acts only locally on peripheral opioid receptors in the gut wall. This largely prevents the opioid from binding to these receptors, inhibiting the oxycodone from exerting its effects on the digestive system and significantly reducing the risk of opioid-induced constipation, thus maintaining normal bowel function.^{Error! Bookmark not defined.,Error! Bookmark not defined.,Error! Bookmark not defined.}

Oxycodone, the opioid component of **Targin**, is absorbed by the gut and distributed throughout the entire body. It binds to opioid receptors, including those in the central nervous system (the spinal cord and brain), thus providing analgesia.

“Mundipharma has a strong heritage in pain management and we are proud to introduce **Targin**, the first treatment of its kind to be specifically designed to provide pain control



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whilst significantly improving bowel function and improving the quality of life of patients by minimising the risk and effect of opioid-induced constipation,” concluded Dr Karen Reimer, Mundipharma’s European Research & Development Director. “We trust this novel drug will provide clinicians with an important new option in the management of severe chronic pain.”

– Ends –

Notes to Editors:

About *Targin*

Targin is a combination of the strong opioid analgesic oxycodone and the opioid receptor antagonist naloxone in a prolonged-release tablet formulation.

Targin has been clinically proven to provide comparable analgesic efficacy to that of oxycodone, whilst significantly counteracting opioid-induced constipation, a class effect associated with all opioids. *Targin* is a prolonged-release formulation providing twice-daily dosing.

Targin received approval on 27th October 2008 via the Mutual Recognition Procedure for 13 European countries (*Austria, Belgium, Cyprus, Denmark, Finland, Germany, Iceland, Ireland, Luxembourg, Netherlands, Norway, Sweden, United Kingdom) for the treatment of severe pain and to counteract opioid-induced constipation. *Targin* will be launched in European countries from 2009 onwards. *Targin* was launched in Germany in 2006 via an expedited approval procedure.

About oxycodone

Oxycodone is a strong opioid analgesic, used for the treatment of severe chronic pain. Its efficacy has been demonstrated across a broad spectrum of severe pain states such as somatic and neuropathic pain.¹¹

About naloxone

Naloxone is an opioid receptor antagonist that, when taken orally, has negligible systemic bioavailability (<3%),¹² providing a full inhibitory effect on local opioid receptors in the gut – counteracting opioid-induced constipation – without impacting on the centrally acting analgesic efficacy of oxycodone.

The oxycodone/naloxone combination will be marketed across Europe under the brand names *Targin* and *Targinact*TM.

About Mundipharma International Limited

The Mundipharma/Napp/Norpharma independent associated companies, including Mundipharma, Purdue and Napp, are privately owned companies and joint ventures covering the world's pharmaceutical markets. The companies worldwide are dedicated to bringing to patients with severe and debilitating diseases the benefits of novel treatment options in fields such as severe pain, haemato-oncology and respiratory disease. Prolonged release oxycodone / naloxone was developed by Mundipharma Research. For more information: www.mundipharma.co.uk



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