Is 15 Minutes Now a Disorder? When Will We Learn

By: Timothy Cheney | Chooper's Guide | August 17, 2012

Clever and deceptive marketing has evolved into an art form over the past several decades and has become the standard for much of the pharmaceutical industry for launching new sedative and analgesic drugs into the marketplace. Soothing names such as Ambien, Lunesta and now Intermezzo subliminally convey to the sleep-deprived user feelings of calm, peace and safety. How could a drug marketed as a sleeping aid be construed as dangerous with names such as these and who will be embarrassed to admit that they are taking a drug to sleep that has been shamelessly and insidiously promoted on primetime TV with images such as a floating butterfly and accompanied with soothing music? These no longer sound like a substance that has a high abuse and addiction potential. For example, Ambien, which has the same active sedative ingredient Zolpidem as Itermezzo**,** is a sedative-hypnotic belonging to the imidazopyridine class of non benzodiazepine drugs and has a high psychological and physical dependence potential. Although they are different in structure to the benzodiazepine family, this class of sedatives binds to the same $GABA_A$ receptors in the same location of the brain as the benzodiazepine class. The name Ambien (ami bien) either by design, or by sheer serendipity, is derived from French and its translation is "good friend." The pharmaceutical manufacturer just happened to be French. Okay, I think I've got it: Take these sleeping "aids " (they are no longer pills because the word pill can be associated with "pill head," "pill addict" and addiction) and they soon will acquire 'good friend' status because they will knock you out in fifteen minutes. But wait , there is more. They are not just friends, they are really good friends because they give you more: they may give you amnesia, somnambulism, possibly cause hallucinations and, because who just wants to have one friend when you can have many friends, you may become first psychologically and then physically dependent and that means you will be taking many more. However, if you decide you don't like your 'friends' anymore, you have a problem. You can't just abruptly terminate your relationship and leave. Instead, you have to stick around for a very uncomfortable separation that involves insomnia, anxiety and possibly convulsions or perhaps a trip to a rehab, which will set you back $20 -30K. In my book, these are definitely, 'Good Friends.'

Enter, Intermezzo, developed by California based Transcept and now marketed and sold by our old friends at Purdue Pharma, who after a substantial investment secured the initial marketing rights, in April of 2012. This collaboration makes sense in the boardroom as Purdue Pharma has a proven track record in rolling out addictive substances to the marketplace. From the streets of major urban areas and to the back hills of Kentucky, Purdue Pharma is associated with "good product". They are the new millennium's corporate version of the notorious narcotics operation directed by NY heroin dealer, Nicky Barnes, who dominated heroin distribution in much of the northeast in the 70's.

This scenario reeks of déjà vu. This powerful, fast acting, four hour sedative hypnotic is positioned to capture the attention of a different segment of the untapped substance use/abuse population. This is

not their first attempt at off-label marketing for addictive substances. Purdue Pharma, the manufacturer of Oxycontin, aka "hillbilly heroin", has the distinct yet dubious honor of being the first 21st century pharmaceutical firm that single handedly created an opioid addiction epidemic that has transcended all socioeconomic barriers costing society billions of dollars with an unprecedented mortality rate and countless lives and families destroyed. With revenues of approximately $3.2 billion in 2011 and proceeds from Oxycontin sales at an estimated $2.9 billion, one might conclude that their core business model is the manufacture and sale of addictive substances using high powered, highly deceptive marketing practices to create a psychologically and physically dependent customer base. These are the same tactics, basically, as the well known drug dealer in the schoolyard scenario which now is strictly enforced with harsh criminal sanctions. America is a big school yard and our teachers went to sleep at the wheel leaving us as prey to these sociopathic cartels masquerading as legitimate businesses, aka pharmaceutical companies. As Don Corleone schooled his son, Sonny, in the Godfather – "Lawyers can steal more money with a briefcase than a thousand men with guns and masks." This statement written for Hollywood seems to be a case of life imitating fiction. It would be an interesting study to compare the earnings before income taxes (EBIT) of the pharmaceutical companies with the cartels and filter the income by product line.

Oxycontin, active ingredient oxycodone, was initially deliberately marketed as a potent pain killer with a low abuse and addiction potential. Previous oxycodone medications such as Percodan and Percocet were manufactured with lower oxycodone content and both contained other ingredients, aspirin and caffeine and acetaminophen respectively which significantly reduced their abuse potential due to the side effects of the diluents. Oxycontin targeted and successfully captured a significant segment of the illicit opioid marketplace as it contained significantly more oxycodone per dosage and it was pure and unadulterated oxycodone. This, in my estimation, was not an oversight. It was deliberate and strategically brilliant. Company executives were subsequently prosecuted for the deliberate misrepresentation and an award of $630 million was handed down. Although that is a tidy little sum for lying, it, in actuality, is a small percentage of the overall historical gross revenues derived from Oxycontin sales and is a onetime charge. In the corporate business world, this is referred to as the cost of doing business. The old adage - I would rather ask for forgiveness than ask for permission - seems to be their modus operandi and they continue to get away with it both with the FDA and with the consumer.

In June of 2012, it was reported that Purdue Pharma would launch the most massive pharmaceutical marketing campaign in recent history anticipated to be well over $100 million to launch Intermezzo into the marketplace and, according to the slideshow (see attached PDF File) 8K ex. 99.1 released in March of 2012, Purdue Pharma would be hiring 275 additional sales representatives. Its reach will extend far beyond the alleged targeted population, as intended. And, as Intermezzo is classified as a Schedule IV substance, it will not be subject to the same level of scrutiny that other high abuse risk schedule II and III substances.

Intermezzo, an Italian word meaning interlude or intermission, and associated with dramatic musical interludes in festivities and opera, originated in the 1500's. Intermezzo will be marketed as a short acting sedative-hypnotic to address the problem of broken sleep with persons suffering from insomnia or sleep disturbances. The active ingredient is Zolpidem, the same as in Ambien, and therefore has the same side effects, psychological dependence and physiological addictive properties. However it poses a

much greater threat for recreational abuse and addiction due to its sublingual method of administration which allows the drug's effects to be experienced much more quickly than if swallowed. The FDA advises to take Intermezzo while in bed due to its rapid onset. In the world of the substance abuser, there are four factors that are important in determining drug of choice: drug effect, length of effect, method of administration and time of onset of effects. Intermezzo satisfies all four requirements admirably. It produces a sedative high, only lasts 4 hours which makes it a good party and club drug, can be placed under the tongue eliminating the need for needles and pipes or ruining your nose and it gets into your bloodstream very quickly. It is a home run for teenagers who have to look straight when they get home just as Fentanyl , a short acting and highly potent opioid, is for the medical professional. Will Intermezzo become the street addicts' drug of choice? Most likely, no as it is a sedative hypnotic rather than an opioid or behavioral stimulant (Meth, Cocaine). However, does it have the potential to create a new marketplace for the naïve and stigma-conscious user population and could it easily become an extremely popular recreational drug for the young and a quick sedative fix for the professional or housewife? Yes. Barring further regulation, look for it to become a gateway drug and for an increased incidence of sedative hypnotic use, abuse and addiction nationally.

An interesting and disturbing finding can be discovered buried in the FDA medical review of efficacy data on page 306 of the 403 page document, in this instance for Lunesta, but as they are all of the same family, it can be applied to this class of sedative hypnotics. In the longest, largest Phase III trial, patients in the Lunesta group reported falling asleep an average of 15 minutes faster and sleeping an average of 37 minutes longer than those in the placebo group. However, on average, Lunesta patients still met criteria for insomnia and reported no clinically meaningful improvement in next-day alertness or functioning. Stripped of the marketing hype, it would seem that the risks would outweigh the rewards on this one, but maybe 37 minutes more sleep is in this fast-paced world where immediate gratification has become the standard is an acceptable risk. And, I might ask is 15 minutes the differential between normal and a disorder? And, who established this diagnostic criteria?

Take a moment to think about this because the numbers appear to indicate that no one has. Eight to ten percent of individuals have the genetic risk factor to develop a substance abuse disorder. Rather than acknowledging this when evaluating new drugs, we are allowing big pharma to use the media to manipulate the perception of what constitutes a disorder and therefore create a new market. This new disorder is cleverly named MOTN (Middle of the Night) insomnia. You would think they could throw a Greek or Latin term in as the cost will be $5 to $6 per pill. My apologies, I meant 'aid'. Their payoff is billions of dollars and the consumers' payoff is getting to sleep fifteen minutes faster, sleeping thirty seven minutes longer with no self-reported derived benefits and paying higher health care costs to treat the 8 to 10% of the population who can't handle the substance. Incredible!!

I, for one, am outraged at the level of sheer ignorance, greed and apathy at the legislative level and appalled at the naivety and lack of fundamental pharmacological knowledge of the members of the American medical profession. Additionally, prescribing practices for these "sleep aids" tend to be lax and not confined to cases where secondary or co-morbid conditions have been investigated and eliminated as causal factors. This article is not meant to discount the appropriate prescribing of sedative hypnotics for those afflicted with primary insomnia, but rather to serve as an indictment of the pharmaceutical industry for reckless endangerment and premeditated misrepresentation and of the government regulating authorities for gross negligence. This class of sedative- hypnotics has the same

risk for abuse and the same addiction liability as their cousins, the benzodiazepines, and therefore should be classified as Schedule III substances.

The old adage that no one ever died from lack sleep appears to be true as statistics indicate that insomnia is correlated with increased longevity, whereas individuals who take sleeping pills have a higher mortality rate.

Once again, we have opened the gate to the school yard and let the drug dealers set up shop. Oh, the translation for Lunesta, is 'your moons.' How sweet. I definitely feel safe now.

Note: I have attached a PDF file of a slideshow of Trancept's ex. 991 contained in their 8k dated March 13, 2012. Please be seated before you read this. This is a cold and calculating document that exposes the pharmaceutical industry's feasibility assessment process and their strategy for delivering a new drug to the marketplace.