Overactive bladder, under scrutiny, gets a new treatment

A cop is directing traffic when the urge to urinate suddenly strikes and, overcome, she abandons a busy intersection in search of a restroom. The solution for “always having to go,” according to the advertisement in which she appears, is medication for “overactive bladder.” In no time, she’s back on the job, no longer in any need for those vexing bathroom breaks. In reality, however, many people diagnosed with overactive bladder don’t benefit from drugs. And despite the approval in June of a first-of-its-kind drug for the condition, the debate continues as to whether the term itself is a confusing catchall.

Overactive bladder describes a pressing need to urinate due to bladder spasms or contractions, with symptoms that can include repeated trips to the bathroom—even at night—and incontinence. Patients diagnosed with this disorder are typically asked to try behavioral changes, such as decreasing fluid intake and altering diet, as well as exercises to strengthen the pelvic floor muscles to reduce or decrease leakage. If that doesn’t work, doctors will prescribe medications that target the symptoms.

Currently, experts estimate that between 30 million to 50 million people in the US alone are diagnosed with ‘overactive bladder’. But many experts worry that the term casts too wide a net.

In a recent commentary, Kari Tikkinen, a urologist at McMaster University in Hamilton, Canada, argues that lumping the symptoms together is an oversimplification (*Eur. Urol.* 61,

746–748, 2012). “Calling it one disease, you fail to recognize that there are many reasons for the symptoms, from neurologic dysfunction to prolapsed uterus to prostate disorders that have nothing to do primarily with the bladder,” says Tikkinen. “So there’s a huge risk that you overtreat people with these drugs. The symptoms should be studied individually to develop effective medications and therapies.”

But Alan Wein, head of urology at the University of Pennsylvania Perelman School of Medicine in Philadelphia, who helped coined the term in 1997, defends the diagnosis. “Overactive bladder is a patient-friendly term,” he says. “We thought it might get more people that had this condition to be treated.”

Antimuscarinics, the current treatment standard, relax the bladder’s smooth muscle, reducing involuntary contractions and subsequent leaks. The six antimuscarinics on the market, including the gel Anturol (oxybutynin), from New Jersey-based Antares Pharma, approved last December, all have “reasonable effect,” says Roger Dmochowski, a urologist at the Vanderbilt University Medical Center in Nashville, Tennessee. But, he adds, about 30% of people who take them see no response.

Expanding options

On 28 June, the US Food and Drug Administration approved Astellas Pharma’s Myrbetriq (mirabegron), the first in a new class of drugs to treat overactive bladder. The once-

daily pill, a beta-3 adrenergic agonist, relaxes the bladder muscle during filling, improving storage capacity. In phase 3 studies submitted by Astellas to the agency, the drug from the Tokyo-based pharmaceutical company decreased urinations by about 1.7 episodes per day on average from a baseline of about 12, compared with a 1.2-episode reduction with placebo, and cut daily leakage episodes nearly in half, from a baseline of about 3 to 1.5, compared with a reduction of only 1 with placebo. More beta-3 adrenergic agonists are in the pipeline, such as AltheRx Pharmaceuticals’ solabegron and Kissei Pharmaceuticals’ ritobegron.

Still, some onlookers remain unsuayed by that data. “The studies show these drugs barely work,” says Kate Ryan, program coordinator at the National Women’s Health Network, a nonprofit advocacy organization in Washington, DC. “These drugs reduce the frequency by less than once per day compared to the placebo, and that is not enough to make a meaningful difference in anyone’s life.”

Scientists are on the hunt for urine and blood biomarkers for overactive bladder that could refine the diagnosis and lead to more targeted therapies. In the meantime, though, clinicians need to be better about creating reasonable expectations, says Dmochowski. “Patients think that medication is going to cure them,” he says. “With current therapies, the majority will be benefited, but not cured.”

Alisa Opar

Study finds up to \$5 billion in potential trial cost savings

Extraneous procedures in clinical trials are costing the drug industry up to \$5 billion each year. That’s according to a new analysis from the Tufts University Center for the Study of Drug Development, which found that tests not linked to key efficacy or safety trial goals can account for as much as 20% of a clinical study’s budget.

According to Ken Getz, who authored the report, if trial sponsors “directly tie the design of their protocols to their primary endpoints so that only useful data is gathered,” they could stand to save an average of \$260,000 per phase 2 clinical trial and \$1.7 million per phase 3 study on the direct costs of lab tests or participant questionnaires. For example, in a trial looking at a new obesity medicine, measuring blood sugar could be considered a surplus procedure if only changes in body weight and lipid profiles were defined as the primary and secondary endpoints, respectively.

Getz came to his conclusions after analyzing some 22,000 protocol procedures from a total of 117 mid- and late-stage trials sponsored by 15 different drug companies. He reported the findings of the study, which was funded by the New York-

based software firm Medidata Solutions, on 26 June at the Drug Information Association annual meeting in Philadelphia.

Trimming superfluous procedures within trials could even have added cost-cutting benefits, says Christine Pierre, president of RxTrials, a clinical research organization based in Ellicott City, Maryland. In addition to the direct money saved by not running extra tests, more efficient study designs could help lower expenses related to patient recruitment and retention, she notes. “If we can increase enrollment by streamlining procedures, then we can not only impact patient’s willingness to participate, but we might also improve their adherence to the protocol,” Pierre says.

But Steven Goodman, an epidemiologist at Stanford University in California and editor of the journal *Clinical Trials*, worries about the consequences of paring trials down too much, noting that extra information can inform future studies or come in handy in case such data is requested by regulatory agencies. “On the surface it may look like certain procedures do not provide necessary measurements, but this data can later be mined,” he says.

Kathleen Raven