DRUGMonitor

Brief summaries of recent drug approvals, interactions, and adverse events

Medicare vs VA—VA Wins

If Medicare spent money on drugs the way the VA does, it could save millions of dollars without lowering the quality of what patients get, according to a study by researchers from the VA Center for Health Equity Research and Promotion, the University of Pittsburgh Graduate School of Public Health, and the University of Pittsburgh School of Pharmacy, all in Pittsburgh, Pennsylvania; and The Dartmouth Institute for Health Policy and Clinical Practice in Lebanon, New Hampshire.

The researchers looked at the percentage of patients taking oral hypoglycemics, statins, and angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers (ARBs) who filled brand-name drug prescriptions. They also measured the percentage of patients taking long-acting insulins who filled analog prescriptions.

Analyzing data on 1,061,095 patients receiving benefits from Medicare Part D and 510,485 veterans with diabetes, the researchers estimated that, across the 4 medication groups studied, Part D spending would have been $1.4 billion less (39%) in 2008 if Medicare use of brand-name drugs had mirrored VA use during the study period. Conversely, if VA patients were using brand-name drugs at the same rate as the Medicare patients during that period, VA spending would have increased by $108 million, or 57%.

Across the board, Medicare patients were using double to triple the amount of brand-name drugs than were VA patients: 35% vs 13% for oral hypoglycemics, 51% vs 18% for statins, 43% vs 21% for ACE inhibitors or ARBs, and 75% vs 27% for insulin analogs. Although the proportions of each cohort using oral hypoglycemics and long-acting insulins were nearly identical, Medicare patients were less likely to use statins and ACE inhibitors or ARBs than were veterans.

The evidence does not suggest that the differences reflect underuse of brand-name drugs in the VA, the researchers say. "In fact," they note, "the VA provides a reasonable benchmark for use of generic drugs in Medicare, because it performs as well or better than commercial health plans and Medicare on several measures of quality for diabetes and related conditions."

One structural factor that might explain much of the between-system difference, the researchers say, is the VA's ability to promote "therapeutic substitution." That is, interchanging generic drugs in the same class as, but not identical to, single-source, brand-name drugs. That's different from mere generic substitution, they note, in which brand and generic versions of the same drug are substituted.

Part D plans have tools for encouraging clinicians to use less costly drugs, but they have applied them less extensively than has the VA, the researchers say. They suggest that Part D plans may lack the incentives to apply the tools. For example, private Part D plans may lose market share and pharmaceutical manufacturer rebates on drugs if they restrict the use of widely used drugs.

Source: Gellad WF, Donohue JM, Zhao X, et al. *Ann Intern Med.* 2013;159(2):105-114. doi: 10.7326/0003-4819-159-2-201307160-00664.

Delaying Antibiotics for UTI

Many women would be willing to delay antibiotic treatment for urinary tract infection (UTI) symptoms, and that could be a good thing, say researchers from the University of Amsterdam in The Netherlands. In their study of 176 women, of those who chose to delay treatment, 71% saw their symptoms improve or disappear after 1 week.

Patients who experienced painful or frequent urination for ≤ 7 days were recruited from 20 general practitioner (GP) practices in and around Amsterdam. The GPs were requested to ask all patients whether they were willing to delay antibiotic treatment. After 7 days, the patients reported whether their symptoms had improved and whether they had used any antibiotics.

Of the 137 women asked to delay treatment, 51 women (37%) agreed. After 1 week, 28 women (55%) had not used antibiotics and of those, 20 (71%) reported clinical improvement or cure.

The results of the baseline cultures were not known until after the follow-up week. The culture was positive for 26 (51%) of the 51 delaying women and for 58 (67%) of 86 women who did not delay. Of the 20 women who reported improvement or cure, 7 women (35%) had a positive baseline culture.

None of the women in the study developed pyelonephritis. Although the researchers say that placebo arms of randomized trials suggest that cystitis seldom progresses to pyelonephritis, they acknowledge that clinicians sometimes consider the risk of pyelonephritis a reason to treat all women with a suspected UTI.

As far as they know, the researchers say, this is the first study that describes the proportion of women with UTI symptoms who are willing to delay antibiotic treatment. Qualitative research has already suggested that women may not always want to

take antibiotics. Still, GPs in 1 of the 20 practices did not ask any of their 25 patients to delay antibiotic treatment, because they disagreed in principle with the approach. This may illustrate the misinterpretation by clinicians that patients want antibiotics when they actually do not, the researchers suggest.

Women who reported at least considerable pain or who thought they had a UTI were more likely to be included, the researchers say. This suggests that the GPs' decisions about asking women to delay antibiotic treatment were based more on their personal attitudes toward antibiotic prescription than on patient characteristics. They may also be influenced by patients' attitudes and patients' previous health experiences, such as a problematic UTI history.

Placebo arms of randomized trials have shown that 25% to 50% of women presenting with uncomplicated UTI symptoms will recover in 1 week without using antibiotics, the researchers say. Their study findings also accord with those of another trial in which delaying antibiotics reduced antibiotic use by 20% while yielding the same symptom control as immediate antibiotic treatment. In fact, they add, new research is underway that may lead to a change to initial treatment with pain medication.

Source: Knottnerus BJ, Geerlings SE, Moll van Charante EP, ter Riet G. *BMC Fam Pract.* 2013;14:71. doi: 10.1186/1471-2296-14-71.

Dolutegravir Approved to Treat Resistant HIV Infection

A long-awaited new drug for human immunodeficiency virus (HIV) infection, dolutegravir, has been approved by the U.S. Food and Drug Administration (FDA) for adults and, in some cases, children. The drug is a welcome addition for patients who have developed resistance to ≥ 2 classes of antiretroviral drugs.

Dolutegravir is an integrase strand transfer inhibitor indicated for use in combination with other antiretroviral agents. Integrase inhibitors block HIV replication at a crucial stage by preventing the viral DNA from integrating into the genetic material of T-cells.

The FDA approval was based on data from 4 pivotal phase 3 clinical trials involving 2,557 adults. Participants were randomly assigned to receive dolutegravir or raltegravir, each in combination with other antiretroviral drugs, or a fixed-dose combination of efavirenz, emtricitabine, and tenofovir.

Results showed the regimens containing dolutegravir reduced viral loads. For example, in SPRING-2 (ING113086), a study evaluating once-daily dolutegravir and twice-daily raltegravir in 822 HIV-infected, treatment-naïve patients, 88% of dolutegravir-treated patients were virologically suppressed (HIV-1 ribonucleic acid [RNA] < 50 c/mL) by week 48, compared with 86% of raltegravir-treated patients. And in SINGLE (ING114467), a study evaluating once-daily dolutegravir plus abacavir/lamivudine vs once-daily fixed-dose combination of efavirenz, emtricitabine, and tenofovir in 833 HIV-infected, treatment-naïve patients, the proportion of patients who were virologically suppressed at 48 weeks was 88% for dolutegravir and 81% for the fixed-dose combination, a statistically significant difference of 7.4% (95% confidence interval [CI]: 2.5%, 12.3%).

A third study, SAILING (ING111762), compared once-daily dolutegravir with twice-daily raltegravir in 719 patients whose current therapy was not working, but who had not been treated with an integrase inhibitor. Both groups were on regimens that contained up to 2 agents, including at least 1 fully active agent. At week 24, 79% of the patients on dolutegravir were virologically suppressed vs 70% of those on the regimen containing raltegravir, again a statistically significant difference of 9.7% (95% CI: 3.4%, 15.9%).

In the VIKING-3 (ING112574) study, twice-daily dolutegravir was added to the current regimens for 183 adults whose HIV was resistant to multiple classes of HIV medicines, including the integrase inhibitors raltegravir or elvitegravir. After 7 days of treatment, mean HIV RNA levels declined by 1.4 $\log_{10}$ c/mL. At week 24, 63% of patients were virologically suppressed. However, integrase strand transfer inhibitor resistance impeded virologic response in some patients.

A 24-week multicenter trial established the pharmacokinetics, safety, and activity of dolutegravir for treating children aged ≥ 12 years, weighing ≥ 88 pounds, and who had not previously taken integrase inhibitors.

Dolutegravir has been hailed as a *clean* drug, with a low adverse effect (AE) profile and few drug-drug interactions. In general, dolutegravir's tolerability was similar to that of raltegravir and better than the fixed-dose combination of efavirenz, emtricitabine, and tenofovir. When used in first-line therapy, dolutegravir compared favorably with efavirenz, with fewer discontinuations due to AEs. The most commonly reported AEs were insomnia (3%) and headache (2%). Serious AEs included hypersensitivity reactions and abnormal liver function in patients co-infected with hepatitis B or C. ●

Sources: U.S. Food and Drug Administration. FDA approves new drug to treat HIV infection [news release]. U.S. Food and Drug Administration Website. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm364744.htm. Updated August 13, 2013. Accessed September 25, 2013. Tivicay [package insert]. Research Triangle Park, NC: ViiV Healthcare; 2013.

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