DRUG DIALOGUES – Medication news and new medications

Results of clinical trial were buried to change outlook and it is worrying

The debate on full disclosure of clinical trial data has been reignited again with the analysis of a controversial study in adolescents on the use of the antidepressant drug paroxetine. The drug used for the treatment of depression and anxiety, was neither safe nor effective in teenagers—a complete contradiction of the way in which the research was presented in 2001, according to an international team of researchers who did a close analysis of results from Study 29 which was funded by GlaxoSmithKline (GSK) and published in the Journal of the American Academy of Child and Adolescent Psychiatry (JAACAP). The study has come under scrutiny before with previous allegations that the paper had been “ghostwritten” by an outside medical writer hired by the pharmaceutical company. The latest analysis published in The BMJ—which includes data made available after legal challenges in the United States and negotiations between the researchers and GSK, sets the record straight and shows the extent to which drug regulation is failing us. According to their analysis neither paroxetine nor high dose imipramine was more effective than placebo in adolescents with major depression—a result explained by the original study looking at different outcome measures than set out in the initial protocol. They also found a far higher level of serious side-effects, including suicidal thoughts, than had been reported in 2001 with apparent discrepancies in the recording of adverse events, prompting them to conclude that “paroxetine was ineffective and unsafe in this study”. Study author David Healy, professor of psychiatry at Bangor University in Wales, says the original study was representative of “the industry approach towards trials in general”. Healy and the RIAT team believe that “ghost writing, conflicts of interest, and junk research are all serious problems enabled by the lack of complete access to all trial data”. And that these results highlight the clear need for “All Data” not just “All Trials” – the initiative set up to encourage the registration of all trials and reporting of full methods and summary results.

New drug to treat schizophrenia and bipolar disorder

A new drug cariprazine has been approved by the US Food and Drug Administration (FDA) last month to treat schizophrenia and bipolar disorder. The efficacy of cariprazine in treating schizophrenia was demonstrated in 1754 participants in 3 six-week clinical trials. In each of the trials, cariprazine was shown to reduce the symptoms of schizophrenia compared to placebo. The efficacy of cariprazine in treating bipolar disorder was shown in 3 three-week clinical trials of 1037 participants. Cariprazine was shown to reduce the symptoms of bipolar disorder in each of the trials. Cariprazine and all other drugs used to treat schizophrenia and bipolar disorder carries warning alerting healthcare professionals about an increased risk of death associated with the use of these drugs in older people with dementia-related psychosis. Neither cariprazine nor any other drug in this class is approved to treat such patients. The most common side-effects reported by schizophrenia participants were extrapyramidal symptoms, such as tremor, slurred speech, and involuntary muscle movements. The most common side-effects reported by bipolar disorder participants were extrapyramidal symptoms, akathisia, dyspepsia, vomiting, somnolence and restlessness. Cariprazine marketed as Vraylar® by Actavis Pharma Inc.

SGLT2 inhibitors: safety warning

Ketoacidosis and urinary tract infections can result from usage of the antidiabetic drugs SGLT2 inhibitors (canagliflozin and dapagliflozin). This finding which has emerged from US FDA safety review has made the agency add warnings about the risk. Ketoacidosis with SGLT2 inhibitors can occur even if the blood sugar level is not very high. If ketoacidosis is suspected, the SGLT2 inhibitor should be discontinued.

Source: CMC Pharmacy Bulletin, a publication of the Pharmacy Service (DISH), CMC, Vellore.
New treatment for chemotherapy induced nausea and vomiting

The US FDA approved rolapitant tablets early last month to prevent delayed phase chemotherapy-induced emesis. The drug is approved in adults in combination with other antiemetic drugs with initial and repeat courses of emetogenic and highly emetogenic cancer chemotherapy. Rolapitant is a substance P/neurokinin-1 (NK-1) receptor antagonist. Activation of NK-1 receptors plays a central role in nausea and vomiting induced by certain cancer chemotherapies, particularly in the delayed phase. The most common side-effects in patients treated with rolapitant include neutropenia, hiccups, decreased appetite and dizziness. Rolapitant is marketed as Varubi by Tesaro Inc, Massachusetts.

Nivolumab - New Drug for Metastatic NSCLC

The US FDA last month approved nivolumab to treat patients with metastatic non-small cell lung cancer (NSCLC) whose disease progressed during or after platinum based chemotherapy. Nivolumab works by targeting the cellular pathway known as PD-1/PD-L1. By blocking this pathway, nivolumab may help the body’s immune system fight the cancer cells. Earlier this year, the FDA approved nivolumab to treat patients with advanced squamous NSCLC whose disease progressed during or after platinum based chemotherapy. This new approval expands the use of nivolumab to also treat patients with nonsquamous NSCLC. The safety and efficacy of nivolumab for this use was demonstrated in an international, open-label, randomized study of 582 participants with advanced NSCLC whose disease progressed during or after treatment with platinum-based chemotherapy and appropriate biologic therapy. Another drug called pembrolizumab (Keytruda®) with same mechanism as nivolumab was also approved a week before nivolumab for treating NSCLC specifically for patients whose tumors expressed PD-L1. Nivolumab is marketed as Opdivo® by Bristol-Myers Squibb.

Can Diclofenac Patch be Cut to Adjust Dose?

Can I cut 100 mg diclofenac patch to deliver 50 mg of the drug for a paediatric patient? This was one of last month’s drug information queries. Medication patches are available in a limited number of dosage strengths. Occasionally, patients require a different dosage of a medication than the dosages commercially available in patch form. Cutting a patch may be an option to provide alternative doses. However, many patches should not be cut or altered in any way. Some medications are only effective at specific and exact doses; such is the case with fentanyl patches. Additionally, alteration of the patch may interfere with the way it was designed to deliver medication. Even when alteration of a patch is deemed safe and appropriate, clinicians must consider changes that may occur in the adhesive qualities of the patch, as cutting can result in sharp corners or an odd shape. Patches of the reservoir type (eg. durogesic®) should not be cut, as cutting destroys the rate-controlling ability of the membrane and can lead to delivery of the entire drug dose immediately on application. Depending on the medication type, the cutting of a patch that uses a microreservoir system can be safe and appropriate, but some of the reservoirs will be destroyed when the patch is cut; consequently, it cannot be guaranteed, for example, that if a patch is cut in half, 50% of the dose will be delivered to the patient.

Now available—Treatment for Factor X Deficiency

Factor X deficiency is an inherited disorder, affecting men and women equally, where the blood does not clot as it should. Patients with the disorder are usually treated with fresh frozen plasma and plasma derived prothrombin complex concentrates to prevent bleeding. The US FDA last month approved “coagulation Factor X (human) concentrate” for Factor X deficiency. The concentrate which is derived from human plasma, is indicated for individuals aged 12 and older with hereditary Factor X deficiency for on-demand treatment and control of bleeding episodes, and for perioperative management in patients with mild hereditary Factor X deficiency. The safety and efficacy of “coagulation Factor X” was evaluated in multi-center, non-randomized study involving 1 participants (208 bleeding episodes) for treatment of spontaneous, traumatic and menorrhagic episodes. The concentrate was demonstrated to be effective in controlling bleeding episodes in participants with moderate to severe hereditary factor X deficiency. The concentrate is manufactured and marketed as Coagadex® by Bio Products Laboratory Limited in Elstree, Hertfordshire, UK.

Source: CMC Pharmacy Bulletin, a publication of the Pharmacy Service (DISH), CMC, Vellore.