

Help for those with chronic constipation

Prucalopride is a new drug option for adults who do not have adequate relief from laxatives. **Joan Chew** reports

People suffering from chronic constipation who find no help from laxatives can now turn to a new drug which works by stimulating gut movements.

The drug, prucalopride, which goes by the trade name Resolor and is manufactured by Janssen, a subsidiary of pharmaceutical giant Johnson & Johnson, was approved by the Health Sciences Authority (HSA) in February.

It is the first drug in its class available to treat constipation in at least the last five years.

Symptoms of constipation include infrequent bowel movements, hard or lumpy stool, straining, bloating, a sensation of incomplete evacuation after a bowel movement and abdominal discomfort.

About one in four people in Singapore suffer from chronic constipation.

To qualify as being chronic, the symptoms should be present for more than 25 per cent of the time in the last three months, with the first symptom arising six months ago.

There are many causes of constipation including medication, poor bowel habits, low-fibre diets and diseases of other parts of the body that also affect the colon.

Once the secondary causes are ruled out, constipation is usually dealt with through lifestyle changes, such as increasing fluid and fibre in the diet and engaging in regular physical activity, as well as the use of laxatives.

But some 20 to 30 per cent of patients do not get adequate relief even from laxatives, said Dr Daphne Ang, a consultant in the department of gastroenterology at Changi General Hospital.

They would often have to stick to these in the absence of other viable drugs, she said.

This is where prucalopride fills the gap in treatment.

Gastroenterologists and colorectal surgeons say the drug is for chronically constipated patients on whom lifestyle changes and laxatives have not worked.

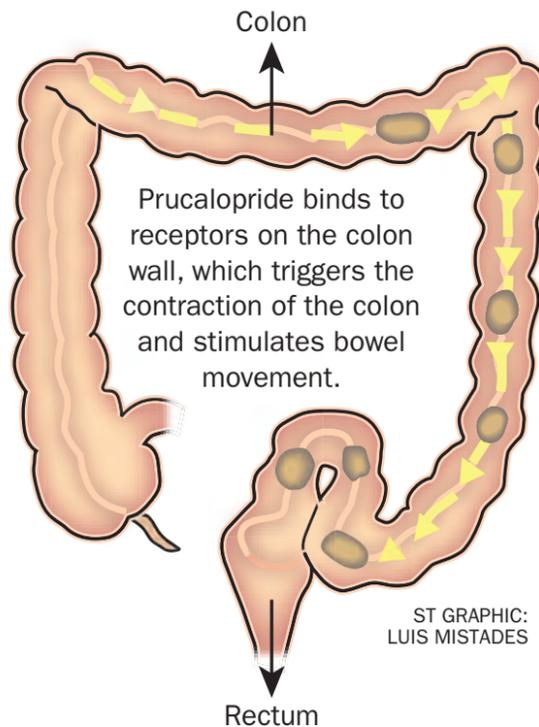
Such patients are normally referred to them by general practitioners and polyclinic doctors.

So far, 50 patients have been prescribed the drug by four doctors at two public hospitals and two private clinics here.

The once-daily medication is given at 1mg dose for elderly patients and 2mg dose for adults and costs \$2 and \$3 each day respectively.

Patients take it for as long as they need it, depending on their symptoms.

But generally, any drug needs to be taken for at least two weeks before it can ease chronic constipation, said Dr Gwee Kok Ann, a consultant gastroenterologist at Gleneagles Hospital.



HOW THE DRUG WORKS

The urge to defaecate follows contractions in the colon to push stool towards the rectum, in a process known as peristalsis.

These contractions occur a few times a day, usually immediately after waking and after meals, but its frequency and duration are often reduced in constipated patients.

Laxatives work either by softening the stool with water, bulking up with fibre, or by stimulating the contraction of intestinal muscles so that the stool moves quickly through the colon to induce bowel movements.

Prucalopride belongs to a class of drugs known as prokinetic agents, which are believed to work in a different way from laxatives.

They act on receptors in the colon to increase the number of muscular contractions and, hence, the frequency of bowel movements.

Older prokinetic agents, such as tegaserod and cisapride, could sometimes lead to heart problems such as cardiac arrhythmia (irregular heart rhythm).

So these have mostly been pulled from use in many countries, including Singapore, said Dr Ho Kok Sun, the president of the Society of Colorectal Surgeons (Singapore).

Just one of them, tegaserod, can still be prescribed here, but under special approval from the HSA, he said.

What differentiates prucalopride from its predecessors is that it is more selective in action, said Dr Reuben Wong, a consultant at the department of gastroenterology and hepatology at National University Hospital.

Even when the drug was given at doses up to five times its recommended dose of 2mg to healthy volunteers in one study, it still did not affect the heart and remained safe for use.

Studies have shown that prucalopride works better than a placebo.

For example, in a trial of 620 patients with severe chronic constipation, published in The New England Journal Of Medicine in 2008, patients

were randomly assigned to receive one of three pills daily: 2mg or 4mg of prucalopride or a placebo.

After 12 weeks of treatment, those on the 2mg pill defaecated on 2.2 more occasions a week and those on the 4mg had 2.5 more, while those on the placebo had only 0.8 more.

The proportion of patients having three or more spontaneous, complete bowel movements per week was 30.9 per cent of the group taking the 2mg pill, 28.4 per cent of the group taking the 4mg pill and 12 per cent of those on the placebo.

In the study, those on prucalopride were also 50 per cent less likely than those on the placebo to use laxatives at the same time.

Prucalopride is usually not prescribed for use at the same time with laxatives.

MILD SIDE EFFECTS

The study observed that patients taking prucalopride were more likely than those on placebo to have the side effects of nausea, abdominal pain, diarrhoea and headache.

These side effects led to drop-out rates of 8.2 per cent of those receiving 2mg of prucalopride, 7.8 per cent of those receiving 4mg of prucalopride and 1.9 per cent receiving placebo.

Still, the authors noted that the majority of these side effects were mild or moderate in severity, occurred mainly during the first day of treatment and were transient.

Dr Gwee said if patients stop taking the drug, it is usually because of side effects such as diarrhoea and abdominal pain.

About a third of the 30 patients he has put on prucalopride opted not to continue with the medication after just one or two days because of the side effects.

But patients should try to stay on the medication for at least two weeks before making a decision on stopping it, as any constipation drug needs at least this amount of time to work and the side effects are transient, Dr Gwee said.

For example, diarrhoea can occur initially when the retained stool are emptied from the colon, but this will go away after that, he said.

Nonetheless, prucalopride should not be a long-term solution, he said.

The main thing is to teach people to get in the habit of emptying their bowels in the morning since it is most active then.

A 39-year-old project manager,

Ms D. Kok, has been relying on laxatives to relieve her bouts of constipation in the last eight years.

She was prescribed prucalopride by Dr Gwee in April and now has bowel movements four to five times a week.

But she is still taking the drug as she

still experiences some bloating.

She said: "Taking laxatives resulted in sharp, violent urges to go and no one likes that because it's not natural."

"The new drug feels milder and so is better for me."

1 in **4**
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