Brand change update:

Ritalin SR now available by Special Access

In response to concerns raised by Medsafe and the Centre for Adverse Reactions Monitoring (CARM), PHARMAC has agreed to allow patients, who experience serious adverse reactions while on Rubifen SR, to return to Ritalin SR under special access.

CHANGING FROM RITALIN TO RUBIFEN

In September 2006, PHARMAC announced that it would cease funding for Ritalin SR (long-acting methylphenidate), a decision mostly affecting children with Attention Deficit Hyperactivity Disorder (ADHD). Instead, Rubifen SR (also long-acting methylphenidate) would be funded, at first along with Ritalin SR, and then as the sole brand of methylphenidate from April 2007. Rubifen was not a new brand; the short acting form was already funded and used by more than 6000 people, at the time of this decision.[1]

Rubifen SR tablets and packaging appear different than that of Ritalin SR, however both brands are considered bioequivalent.

Refer to BPJ Special Edition, March 2007, for more details on the guidelines for medication bioequivalence in New Zealand

Reports begin to emerge of adverse effects following the change to Rubifen SR

CARM received 88 reports of adverse reactions between February and September 2007, when people began to change brands of methylphenidate. Around half of these people claimed a reduction in therapeutic effect with Rubifen SR. In addition, some people reported mood changes, irritability, aggressive or threatening behaviour and unusual psychiatric events shortly after changing to the new brand. This was of particular note in children aged under 17 years.[2]

These reports accounted for less than 2% of patients on methylphenidate SR and most reported adverse reactions occurred within a few days of the brand switch.[3] However, the rate may be higher due to under reporting.

PHARMAC allow a special access subsidy for Ritalin SR

As a result of these reports, Medsafe's Medicines Adverse Reactions Committee (MARC) recommended that PHARMAC make funded Ritalin SR available for patients who experienced serious side effects when they changed to Rubifen SR.[2]

On September 27th, 2007, it was announced that Ritalin SR would be funded for these people on application to PHARMAC on the Ritalin SR Special access form.[3]

NB: Ritalin SR Special Access funding is only being offered for people who had a prior prescription for Ritalin SR, not new patients who started on methylphenidate for the first time after the brand change had occurred.

DEALING WITH BRAND CHANGE

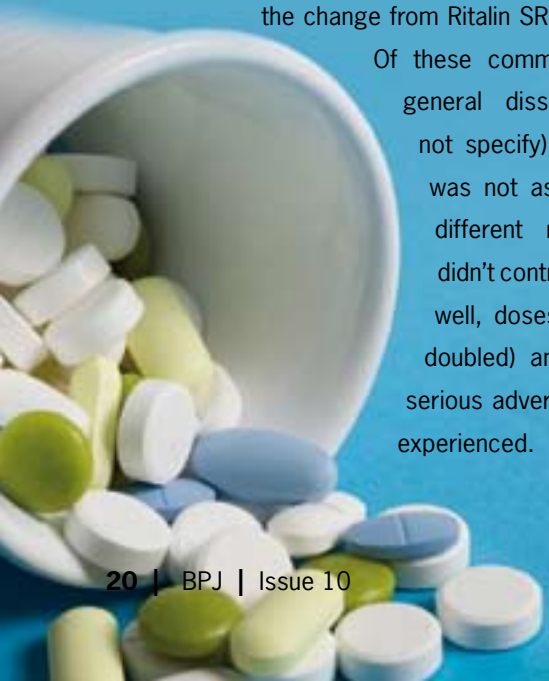
The issues surrounding a brand change become more complex when the drug in question is mainly used in the treatment of mental illness. Consideration must be given to the perception and attitudes of a person receiving treatment for ADHD, and their likely young age, and how this may affect the way they accept a change to their drug therapy, both physiologically and psychologically. One of the main barriers in changing brands of medication is perception of risk by the patient, their family and their caregivers. Studies have found that patients who receive information from their physician or pharmacist about generic substitution are more likely to accept the change.[7]

There is no physiological reason why switching between identical doses of the same drug should result in a different response, however it is unknown what effect drugs such as methylphenidate may have on behavioural responses to change.

Refer to BPJ Special edition, March 2007, for further information on changing to a generic drug

bpac receives anecdotal reports from pharmacists of adverse effects with Rubifen

While assessing pharmacist response to another brand change, we received several spontaneous reports of problems surrounding the change from Ritalin SR to Rubifen SR. Pharmacists were asked to describe any instances of dissatisfaction with brand change. Of the 220 pharmacists who responded, 23 specifically mentioned the change from Ritalin SR to Rubifen SR. Of these comments, 12 were general dissatisfaction (did not specify), ten claimed it was not as effective (e.g. different release profile, didn't control symptoms as well, doses needed to be doubled) and one claimed serious adverse effects were experienced.



IS THERE A PROBLEM WITH RUBIFEN SR?

No obvious cause can be isolated to explain the occurrence of the adverse reactions experienced by people changing from Ritalin SR to Rubifen SR. It is not unexpected that adverse effects are reported after a brand change. This can occur even when the brand does not actually change, for example in one study, nearly half the participants reported subjective differences between their own and study-supplied Ventolin inhalers.[4] Another study assessing acceptance of generic drugs (satisfaction, adverse effects), found significant differences between pharmacological classes of drugs, with less acceptance associated with substitution of drugs acting on the central nervous system.[5]

The brand change from Ritalin SR to Rubifen SR involved the slow release form of methylphenidate 20 mg. This is said to be equivalent to two doses of normal release methylphenidate 10 mg, given four to six hours apart. However there is a lack of evidence of comparisons between the normal and slow release forms. It is claimed that with the slow release form, the release of methylphenidate is slower and the maximum blood level is lower for a more consistent effect. It is theoretically possible that Ritalin SR and Rubifen SR could have different release profiles in some people however, when compared, they were considered to be bioequivalent forms of the same chemical.

Details of CARM reports

CARM has released further information on reports of adverse effects in 56 children who changed from Ritalin SR to Rubifen SR. Symptoms were experienced from a few hours to a few days after the change.[2]

- 75% reported loss of effect
- 55% reported unusual psychiatric events; mood disorders, irritability, hallucinations and suicidal ideations
- 55% reported aggressive and/or oppositional defiant behaviour

Reports of adverse effects in the literature

A literature search using Medline revealed no reports of adverse effects specifically attributable to Rubifen or methylphenidate brand change. It is known that methylphenidate use in children

can be associated with symptoms such as those reported, however this is very rare.[2] The only other country in which the Rubifen brand is marketed is Argentina.

Side effects that can commonly occur when treatment with methylphenidate is first commenced include; nervousness, insomnia, headache, decreased appetite, abdominal pain, nausea, vomiting and minor cardiovascular effects.[6]

An **overdose** of methylphenidate results in overstimulation of the central and sympathetic nervous system and symptoms may include; vomiting, agitation, tremor, hyperreflexia, muscle twitching, convulsions, euphoria, confusion, hallucinations, delirium, sweating, tachycardia and hypertension.[6]

IS IT SAFE TO USE RUBIFEN?

Medsafe has stated that it is satisfied that the two brands of methylphenidate SR are bioequivalent and that no safety issues have been identified at this point.[2] However it is investigating the Rubifen brand and conducting independent testing. AFT Pharmaceuticals, the manufacturer of Rubifen SR, has been asked to urgently provide further data about the quality and safety of their product.

SUMMARY OF ADVICE

The majority of people using Rubifen SR will not experience any adverse effects in addition to ones previously experienced with Ritalin SR.

Anyone receiving a new prescription for Rubifen SR, as for any brand of methylphenidate, should be started at a low dose and increased slowly to allow monitoring of effect and side effects.

If a person previously on Ritalin SR, taking Rubifen SR for the first time experiences major mood changes (e.g. sadness, anxiety, agitation or aggression) or abnormal behaviour or thoughts, the following action is recommended:

- Rapid assessment is required by the specialist multidisciplinary team
- Alternative treatment options should be discussed with patient and family
- Adverse reactions should be reported to CARM
- Special Access funding for Ritalin SR can be applied for if all other treatment options are unsuccessful

Refer to BPJ Issue 3, February 2007, for further information on the management of people with ADHD

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