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# Is remdesivir more powerful against COVID-19 than first thought?

Jill Margo
*Health editor*

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Remdesivir, the first antiviral drug approved for COVID-19 in Australia, may eventually have a wider application than initially thought.

This month it was approved for the emergency treatment of Australians with severe COVID-19. They receive it by intravenous infusion in hospital.

But now there is growing interest in the potential use of remdesivir by people with less severe symptoms and possibly even for use at home for those with mild symptoms.

Potentially, they would deliver the drug directly into their lungs with an inhaler, like those commonly used for asthma.


This month, Gilead got the green light for use of remdesivir in Australia. **AP**

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Australia has deep experience with the development of inhaled antiviral flu drugs and has lessons to share on the roadblocks ahead.

More than 20 years ago, it discovered the flu drug, Relenza, which inhibits viral replication within minutes of arriving in the lungs.

Delivered via an inhaler, it proved effective in both preventing and treating flu, and with much acclaim was marketed globally in 1999.

Gilead Sciences, the Californian company that developed remdesivir, recently started an early phase clinical trial of an inhaled formulation.

"It is testing it for milder disease and may possibly have prophylactic application. Its proposed development echoes the work that was conducted with Relenza," says Dr Phillip Reece, who worked on the drug in Australia.

"Conducting clinical trials with inhaled drugs can be a challenge," says Dr Reece, an honorary senior fellow in the Department of Pharmacology and Therapeutics at Melbourne University.


Conducting clinical trials with inhaled drugs can be a challenge, says Dr Reece **supplied**

"Three large phase III clinical trials were initially conducted with Relenza in patients with existing symptoms in the US, Europe and Australia.

The European and Australian trials were positive and highly statistically significant but the US trial was not."

"The reasons for inter-country differences in effectiveness have never been fully explained."

Dr Reece, now a consultant to the biotechnology and pharmaceutical industries, says while a vaccine acts by enhancing the immune response, remdesivir acts by inhibiting viral replication.

"In doing so, it has the potential for use both as a treatment for patients already infected with COVID-19 and as a prophylactic."

While he is impressed with the data so far, he says its potential use for less severe symptoms is based on the assumption that COVID-19 replicates primarily in the lungs, which is not yet clear.

Dr Reece is an affiliate member of the ARC Centre for Personalised Therapeutics Technologies at Melbourne University, of which Professor Alastair Stewart is director.


Inhaled formulations may be preferred for drugs that don't reach effective lung concentrations or cause adverse effects elsewhere in the body when administered by injections or as tablets, say Professor Stewart. **supplied**

Despite various challenges, they say inhaled remdesivir currently stands out as the antiviral with the best chance of providing a treatment for COVID-19 in a wider spectrum of patients.

"Inhaled drugs have the advantages of targeted and rapid delivery of smaller doses for conditions limited to the lung and are the mainstay of asthma treatment," says Professor Stewart who is also head of the university's Mechanopharmacology Laboratory

"Inhaled formulations may be preferred for drugs that don't reach effective lung concentrations or cause adverse effects elsewhere in the body when administered by injections or as tablets."

Trials have shown intravenous remdesivir reduces the duration of symptoms of COVID-19 infection. It hasn't been shown statistically to reduce mortality.

Earlier this month, Federal Health Minister Greg Hunt said Australia has enough remdesivir in the national stockpile thanks to donations made months ago by the drug's makers.

Should inhaled remdesivir be effective, its production of this formulation would have to be massively scaled-up.

Professor Stewart and Dr Reece say the US government's recent purchase of all available stocks of intravenous remdesivir is a salient reminder of the possible challenge ahead.

Fortunately, smaller doses would be required as the drug is expected to be concentrated in lung sputum rather than distributed throughout the body.

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**Jill Margo** is the health editor. She writes about medicine and health from the Sydney office. Jill has won multiple prizes, including two Walkley Awards and is an adjunct associate professor of the University of NSW, Sydney. *Connect with Jill on Twitter, Email Jill at jmargo@afr.com*

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