

Health Technology Briefing November 2021

Nitazoxanide for treatment of common cold due to rhinovirus or other enterovirus infection

Company/Developer

Romark Laboratories LC

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 27102

NICE ID: 10548

UKPS ID: N/A

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Nitazoxanide is in clinical development for the treatment of the common cold due to rhinovirus or other forms of enterovirus infection in adults and children aged 12 years and older. The common cold occurs amongst all population groups and most people will experience multiple infections a year. Currently, there are no treatment options approved to treat the common cold and most recommended management strategies are ineffective at relieving the associated symptoms.

Nitazoxanide is an anti-viral drug, administered in the form of oral tablets, that targets a wide range of viruses including the enterovirus and rhinovirus. Nitazoxanide works by selectively blocking a viral protein called hemagglutinin to prevent the virus from replicating inside the host cell and prevent the production of infectious viral particles. If licensed, nitazoxanide would provide a treatment option that specifically targets the main causative viruses (rhinoviruses and enteroviruses) that are implicated in common cold.

Proposed Indication

Patients aged 12 years and older with common cold due to rhinovirus and other enterovirus infection.^{1,2}

Technology

Description

Nitazoxanide (NT-300) is a first-in-class, host-directed broad spectrum anti-viral drug, belonging to the class of drugs known as thiazolides, that can inhibit the replication of several RNA and DNA viruses.^{3,4} Thiazolides regulate cellular energy metabolism act at a post-translational level by selectively blocking the maturation of the viral hemagglutinin at a stage preceding resistance to endoglycosidase H digestion. This disrupts the production of infectious viral particles by impairing the intracellular trafficking and insertion of hemagglutinin into the host plasma membrane which is a key step for the correct assembly and exit of a virus from the host cell.⁵

Nitazoxanide is currently in clinical development for the treatment of the common cold due to rhinovirus and other enteroviruses. In the phase III clinical trials (NCT03605862, NCT04489381) participants are given two 300mg nitazoxanide tablets by oral administration twice daily for 5 days.^{1,2}

Key Innovation

Currently, there are no treatments available that can cure the common cold and most treatments are not effective at relieving symptoms. By targeting host factors, nitazoxanide inhibit replication of a broad range of rhinovirus and other enteroviruses that cause the common cold without selecting for resistance.⁶ If licensed, nitazoxanide would provide a treatment option that specifically targets the main causative viruses (rhinoviruses and enteroviruses) that are implicated in common cold.

Nitazoxanide was originally developed and commercialized as an antiprotozoal agent that was later identified as a broad-spectrum antiviral drug and has been repurposed for the treatment of influenza. It has also shown antiviral (viral inhibition) activities against a number of viral infections including rhinovirus and other enteroviruses.⁴

Regulatory & Development Status

Nitazoxanide does not currently have Marketing Authorization in the EU/UK for any indication.

Nitazoxanide is also currently in phase II or III clinical development for the treatment of several other indications caused by bacterial or viral infections including COVID-19 and influenza.⁷

Patient Group

Disease Area and Clinical Need

The common cold is the conventional term used to describe a mild, self-limiting, viral upper respiratory tract infection that affects the nose, throat, sinuses and upper airways.^{8,9} Colds are caused by viruses that spread easily to other people. The most common cause of the common cold is rhinovirus infection, but can also be caused by other forms of enterovirus.¹⁰ The mechanism of common cold transmission occurs through direct contact with an infected individual, touching an object or surface that an infected individual has had contact with, and aerosol transmission of the virus when an infected individual coughs or sneezes.^{8,9} Colds spread most easily among groups of people in constant close contact, such as families

and children in school or day care facilities. They are also more frequent during the winter, although the reason for this is not clear.⁸ The onset of symptoms of the common cold is sudden, reaching a peak at day 2-3, then decreasing in intensity.⁹ The main symptoms include: a blocked or runny nose; a sore throat; headaches; muscle aches; coughs; sneezing; a raised temperature; pressure in the ears and face; loss of taste and smell. Less common symptoms of a cold include: a high temperature (fever); headache; muscle pain; loss of taste and smell; mild irritation of the eyes; a feeling of pressure in the eyes and face; and earache.¹⁰ In adults and older children, symptoms tend to last about a week although cough can persist for up to 3 weeks. Smokers tend to have more severe respiratory symptoms (including cough), and the infection is more prolonged.⁹ Common colds usually clear up without causing any further problems. However, the infection can sometimes spread to the chest, ears or sinuses resulting in complications such as chest infection, middle ear infection or sinusitis.¹¹

The common cold can affect all population groups. It is most common in children and is especially common in younger children. Adults experience an average of 2-3 colds per year, whilst children experience an average of 5-6 colds per year.¹² In 2020-21 there were 571 hospital admissions in England with primary diagnosis of acute nasopharyngitis (common cold; ICD-10 code J00), and 625 finished consultant episodes (FCEs), resulting in 487 FCE bed days.¹³ The population likely to be eligible to receive nitazoxanide could not be estimated at the time of writing this briefing from available published sources.

Recommended Treatment Options

Currently no treatments are available that can cure the common cold, and most treatments are not effective at relieving symptoms.⁶ Patients are advised to manage their symptoms by adhering to the following advice: drinking plenty of fluids; getting adequate rest; eating a healthy diet; taking over-the-counter painkiller and decongestant medicines; using vapour rubs; gargling and taking menthol sweets; using nasal saline drops; taking vitamin and mineral supplements; and getting adequate rest.^{6,14}

Clinical Trial Information

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|-----------------|---|
| Trial | NCT04489381 ; Phase 3, A Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate Efficacy and Safety of Nitazoxanide in the Treatment of Colds Due to Enterovirus/Rhinovirus Infection Phase III – Recruiting Locations: United States Primary completion date: May 2022 |
| Trial Design | Randomised, parallel assignment, triple masking, placebo-controlled |
| Population | N=800; 12 to 120 years; presence of clinical signs and/or symptoms consistent with worsening or stable cold due to enterovirus/rhinovirus infection; patient reported symptoms present that have worsened or remained the same relative to previous day as confirmed by responses to questions in the screening FLU-PRO |
| Intervention(s) | 300mg nitazoxanide tablets (oral administration) |
| Comparator(s) | Placebo tables (oral administration) |
| Outcome(s) | Primary outcome measure: <ul style="list-style-type: none"> Time from first dose to sustained response [Time frame: 21 days] |

| | |
|--------------------|--|
| | See trial record for full list of outcome measures |
| Results (efficacy) | - |
| Results (safety) | - |

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|------------------------|---|
| Trial | NCT03605862 ; A Phase III, Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of Nitazoxanide in the Treatment of Colds Due to Enterovirus/Rhinovirus Infection Phase III – Completed Locations: United States and Puerto Rico Study completion date: February 2019 |
| Trial Design | Randomized, double-blind, placebo-controlled |
| Population | N=1765; adults and children aged 12 years and older; clinical signs and/or symptoms consistent with an acute illness compatible with enterovirus/rhinovirus infection; negative rapid influenza test; onset of illness no more than 40 hours before enrolment in the trial |
| Intervention(s) | 300mg nitazoxanide tablets (oral administration) |
| Comparator(s) | Placebo tablets (oral administration) |
| Outcome(s) | Primary outcome measure: <ul style="list-style-type: none"> Time from first dose to symptom response over 21 days of follow-up based upon the FLU-PRO instrument [Time Frame: up to 21 days] See trial record for full list of outcome measures |
| Results (efficacy) | - |
| Results (safety) | - |

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| Estimated Cost |
| The estimated cost of nitazoxanide is not yet known. |

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| Relevant Guidance |
| NICE Guidance |
| <ul style="list-style-type: none"> NICE clinical guideline. Respiratory tract infections (self-limiting): prescribing antibiotics (CG69). July 2008. |
| NHS England (Policy/Commissioning) Guidance |
| No relevant guidance identified. |
| Other Guidance |

- Public Health England (PHE). Guidelines for PHE health protection teams on the management of outbreaks of influenza-like illness (ILI) in care homes. 2020.¹⁵
- NICE Clinical Knowledge Summary. Common cold. 2016.⁹

Additional Information

Romark Laboratories L.C. did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

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- 2 Clinicaltrials.gov. *Trial to Evaluate Efficacy and Safety of Nitazoxanide in the Treatment of Colds Due to Enterovirus/Rhinovirus Infection*. Trial ID: NCT04489381. 2020. Status: Recruiting. Available from: <https://clinicaltrials.gov/ct2/show/NCT04489381> [Accessed 28 April 2021].
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- 10 NHS Inform. *Symptoms of a common cold*. 2021. Available from: <https://www.nhsinform.scot/illnesses-and-conditions/infections-and-poisoning/common-cold#symptoms-of-a-common-cold> [Accessed 02 November 2021].

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- 13 NHS Digital. *Hospital Admitted Patient Care Activity 2020-21*. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2020-21> [Downloaded 16 September 2021].
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