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Horizon Scan

Emerging Antiviral Drugs to Prevent or Treat Influenza

Key Messages

What Is the Issue?

- There is a need to identify drugs currently in development (pipeline drugs) intended to prevent or treat influenza.
- Specifically, policy-makers would like to identify those drugs that have ongoing or recently completed phase II or phase III randomized controlled trials (RCTs) and are not yet approved for use by Health Canada for influenza.

What Did We Do?

- An information specialist did a tailored literature search across major databases to identify relevant RCTs on antiviral drugs for influenza, focusing on information published in English since January 1, 2020, and completed on November 8, 2024.

What Did We Find?

- We identified a total of 17 emerging drugs in 26 completed or ongoing RCTs, mainly testing treatments for adults with uncomplicated influenza, with some studies including children and adolescents.
- The evidence included 2 prevention studies and 3 challenge studies for influenza.
- Most drugs were compared to a placebo and the number of participants in these trials ranged from 46 to 5,000.

What Does It Mean?

- There are promising new drugs in development for treating adults with uncomplicated influenza.

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About This Document

This report provides information on pipeline drugs intended to prevent or treat influenza. Specifically, it identifies drugs that have completed phase II or phase III RCTs and are not approved for use by Health Canada for influenza. In addition, it identifies drugs that have ongoing phase II or phase III RCTs. It is important to note that this report is not a systematic review and does not describe results nor does it include a critical appraisal of the identified studies. This document is not intended to provide recommendations or advice.

Objective

To identify and describe the study and population characteristics of ongoing or recently completed phase II or phase III RCTs that evaluate drugs to prevent or treat influenza and are not currently approved by Health Canada for this indication.

Research Question

What antiviral drugs are in the pipeline for influenza A or B?

Methods

Literature Search Strategy

An information specialist conducted a literature search on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, ClinicalTrials.gov, and Health Canada's Clinical Trials Database. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevance. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research question and selection criteria. The main search concepts were antivirals or other anti-influenza drugs and influenza. Search filters were applied to limit retrieval to RCTs or controlled clinical trials. Retrieval was limited to the human population. For the Embase search, retrieval was also limited to conference abstracts. The search was completed on November 8, 2024, and limited to English-language documents published since January 1, 2020.

Selection Criteria

The studies of drugs to prevent or treat influenza were selected based on the inclusion and exclusion criteria shown in Table 1 and if the drugs of interest were antiviral drugs or drugs with antiviral-like properties.

Several articles obtained through the grey literature search were reviewed to identify new molecules.[1-6]

Table 1: Selection Criteria

Source of information	Inclusion criteria	Exclusion criteria
MEDLINE	Phase II and phase III RCTs	Studies of drugs that have already been approved in Canada to treat or prevent influenza Studies of drugs that are already approved for other indications in Canada and potentially repurposed for influenza in the future Studies of vaccines, devices, traditional herbs or medicines, natural health products, and dietary supplements Dose finding studies or pharmacokinetics or pharmacodynamics studies Drugs that are no longer in development according to the manufacturer's website information or other
Embase	Conference abstracts of phase II and phase III RCTs	
ClinicalTrials.gov	Phase II and phase III interventional studies that are completed, active, recruiting, or not yet recruiting Estimated primary completion date after January 1, 2020	The exclusion criteria previously mentioned Studies that are withdrawn, suspended, terminated, or with unknown status Studies terminated early due to futility

RCTs = randomized controlled trials.

Results

A total of 17 drugs (Table 2) with 26 RCTs, completed or ongoing, were identified. Of these, 5 drugs are marketed in 1 or more countries. Many RCTs were treatment studies and included adults with uncomplicated influenza. One treatment study included children aged 2 to 11 years and 1 treatment study included children aged 6 months to 2 years. Five studies included adolescents aged 12 to 17 years.

There were 2 prevention studies and 3 challenge studies for influenza. In 1 challenge study, the 2009 pandemic strain of influenza A (influenza A/California/07/2009 H1N1) was used to inoculate healthy volunteers.[7]

The emerging drugs were compared to an active control in 5 studies and the remainder were compared to placebo. The study sample size ranged from 46 to 5,000 participants.

The characteristics of the RCTs are captured in Appendix 1.

Table 2: Drugs in the Clinical Pipeline

Drug	Manufacturer	Drug type
CC42344	Cocrystal Pharma, Inc.	Antiviral (PB2 inhibitor)
CD388	Cidara Therapeutics	Antiviral (neuraminidase inhibitor)
Deunoxavir marboxil (ADC189)	Simcere Pharmaceutical Group Limited	Antiviral (PA inhibitor)
Enisamium (FAV00A; Amizon)[a]	Farmak	Antiviral (RNA synthesis inhibitor)
Favipiravir (T-705; Avigan)[b]	Toyama Chemical Co., Ltd.	Antiviral (PB1 inhibitor)

Drug	Manufacturer	Drug type
GP681	Jiangxi Qingfeng Pharmaceutical Co. Ltd.	Antiviral (PA inhibitor)
Ingavirin[c,d]	Valenta Pharmaceuticals JSC	Antiviral (NP inhibitor)
MHAA4549A	Genentech, Inc.	Monoclonal antibody
Neumifil (HEX17)	Pneumagen Ltd.	Antiviral (carbohydrate binding module)
Norketotifen	Emergo Therapeutics, Inc.	Antihistamine (metabolite of ketotifen)
Nitazoxanide (Alinia)[e]	Romark	Antiprotozoal
Onradivir (ZSP1273)	Raynovent	Antiviral (PB2 inhibitor)
Raphamin (MMH-407)[c]	Materia Medica Holding	Antiviral (MHC inhibitor)
Seloxavir marboxil (ZX-7101A)	Zenshine Pharma	Antiviral (PA inhibitor)
Umifenovir (DB13609; Arbidol)[c,f]	Pharmstandard	Antiviral (HA-induced membrane fusion inhibitor)
VIS410	Visterra Inc.	Monoclonal antibody
XC221	Valenta Pharm JSC	MOA undefined

HA = hemagglutinin; MHC = major histocompatibility complex; MOA = mechanism of action; NP = nucleoproteins; PA = polymerase acidic protein; PB1 = polymerase basic protein 1; PB2 = polymerase basic protein 2; RNA = ribonucleic acid.

[a]Available in 11 countries in eastern Europe.

[b]Available in Japan.

[c]Available in Russia.

[d]Also known as pentanedioic acid imidazolyl ethanamide; IEPA; ingamine; pentanoic acid; or vitaglutam.

[e]Available in the US.

[f]Available in China.

Summary

A search was conducted to identify phase II and phase III RCTs that evaluated emerging drugs to prevent or treat influenza. A total of 26 RCTs were retrieved which included 17 emerging drugs.

The pipeline for drugs to treat adults with uncomplicated influenza is promising. There is a limited number of studies specific to the prevention of influenza, the treatment of severe influenza, and in children aged 17 years and younger.

Interpretation of the findings of the bulletin must take into consideration the following limitations:

- The search for RCTs was not systematic. The list may be incomplete and missing studies of drugs that would fulfill the inclusion criteria.
- The status of the identified drugs may have changed since the completion of the literature searches. Some drugs may no longer be in development.
- The published or posted results were not reviewed to determine if they were favourable to the identified drugs; hence, the list may include RCTs with negative findings.

References

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Appendix 1: Ongoing and Completed Randomized Controlled Trials

Please note that this appendix has not been copy-edited.

Table 3: Ongoing Randomized Controlled Trials (Active, Recruiting, or Not Yet Recruiting)

Intervention(s)	Comparator(s)	Study Design, Location(s), and Sample Size	Study Population	Estimated Primary Completion Date	ClinicalTrials.gov Reference
Phase II					
CC42344	Placebo	Single centre, double-blind UK N = 96	Adults (18 to 55 years) – challenge study for influenza A	June 2024	NCT06160531
CD388	Placebo	Multicentre (57 sites), double-blind US, UK N = 5,000	Adults (18 to 63 years) not at risk for influenza complications – prevention study	September 2025	NCT06609460
Favipiravir (T070; Avigan) and other antiviral drugs (includes laninamivir)	No treatment and against each other	Multicentre (4 sites), open-label, adaptive, platform trial 4 countries N = 3,000	Adults (18 to 60 years) with early symptomatic uncomplicated influenza A or B	01 January 2027	NCT05648448
Phase III					
Deunoxavir marboxil (ADC189)	Baloxavir marboxil	Multicentre, double-blind China N = 165	Children (2 to 11 years) with influenza A or B	31 December 2024	NCT06507813
GP681	Placebo	Multicentre, double-blind Location NR N = 328	Adults and adolescents (12 and older) with influenza at high risk of influenza complications	30 December 2025	NCT06573008
GP681	Placebo	Multicentre, double-blind Location NR N = 748	Adults and adolescents (12 years and older) for post-exposure prophylaxis against influenza	30 July 2027	NCT06574503
Seloxavir marboxil (ZX-7101A)	Placebo	Multicentre, double-blind China N = 360	Adolescents (12 −17 years) with uncomplicated influenza	30 November 2024	NCT06099873

NR = not reported.

Table 4: Completed Randomized Controlled Trials With Published or Posted Results

Intervention(s)	Comparator(s)	Study Design, Location(s), and Sample Size	Study Population	Key Outcome	ClinicalTrials.gov or PubMed Reference
Phase II					
MHAA4549A combined with oseltamivir	Placebo combined with oseltamivir	Multicentre (68 sites), double-blind 18 countries N = 166	Adult inpatients (18 to 95 years) with severe influenza A infection	Time to normalization of respiratory function	Lim et al. 2020
Neumifil (HEX17)	Placebo	Single centre, double-blind UK N = 104	Adults (18 to 55 years) – challenge study for influenza	Incidence of symptomatic influenza	NCT05507567 Kitson et al. 2024
Onradivir (ZSP1273)	Placebo	Multicentre (20 sites), double-blind China N = 205	Adult outpatients (18 to 65 years) with acute uncomplicated influenza A	Time to alleviate influenza symptoms	Yang et al. 2024
VIS410	Placebo	Single centre, double-blinded Belgium N = 46	Adults (18 to 45 years) – challenge study for influenza (used a 2009 pandemic strain of influenza A)	Viral load	Sloan et al. 2020
Phase III					
Favipiravir (T-905; Avigan)	Placebo	Multicentre, double-blind 14 countries N = 855	Adults (18 to 80 years) with acute influenza-like illness	Time to alleviation of symptoms and resolution of fever	Hayden et al. 2023
Nitazoxanide (Alinia)	Placebo	Multicentre (38 sites), double-blind 3 countries N = 1,030	Adults and adolescents (12 years and older) with uncomplicated influenza A or B	Time from first dose to symptom response	NCT03336619
Nitazoxanide (Alinia) combined with Oseltamivir	Oseltamivir	Single centre, blinded India N = 67	Adult inpatients (age range NR) with seasonal influenza	Time for resolution of fever	Koul et al. 2024
Raphamin (MMH-407)	Placebo	Multicentre (26 sites), double-blind Russia N = 240	Adult outpatients (18 to 70 years) with acute respiratory viral infection	Time to resolution of symptoms	NCT04244084
Umifenovir (DB13609; Arbidol)	Oseltamivir	Multicenter (14 sites), open label China N = 412	Adult outpatients (18 years and older) with suspected influenza	Time to normal body temperature	Bai et al.2023

Intervention(s)	Comparator(s)	Study Design, Location(s), and Sample Size	Study Population	Key Outcome	ClinicalTrials.gov or PubMed Reference
Phase II and III					
Seloxavir marboxil (ZX-7101A)	Placebo	Single centre, double-blind, adaptive design China N = 900	Adults (18 to 64 years) with uncomplicated influenza	Time to alleviation of influenza symptoms	NCT05702489 Wang et al. 2024
Phase Unknown					
Enisamium iodide (FAV00A; Amizon)	Placebo	Single centre, blinding NR Russia N = 124	Adult outpatients (aged 18 to 55 years) with influenza and influenza-like illness without risk factors for severe disease	Duration of disease	Pshenichnaya et al. 2021

NR = not reported.

Table 5: Completed Randomized Controlled Trials Without Results

Intervention	Comparator	Study Design, Sample Size, and Location(s)	Study Population	Key Outcome	ClinicalTrials.gov
Phase II					
GP681	Placebo	Single centre, double-blind China N = 216	Adults (18 to 65 years) with uncomplicated acute influenza	Time to alleviation of influenza symptoms	NCT04736758
Norketotifen	Placebo	Multicentre (20 sites), double-blind US N = 315	Adult outpatients (18 to 64 years) with uncomplicated acute influenza	Time to alleviation of the symptoms of influenza-like illness	NCT04610047
Norketotifen	Placebo	Multicentre (18 sites), double-blind US N = 238	Adult outpatients (18 to 64 years) with uncomplicated acute influenza	Time to alleviation of the symptoms of influenza-like illness	NCT04043923
XC221	Placebo	Multicentre (9 sites), double-blind Russia N = 255	Adults (18 to 65 years) with uncomplicated influenza or other acute viral upper respiratory infections	Time to resolution of all symptoms	NCT05030324
Phase III					
GP681	Placebo	Single centre, double-blind China N = 591	Adults and adolescents (12 to 65 years) with uncomplicated acute influenza	Time to alleviation of influenza symptoms	NCT05474755

Intervention	Comparator	Study Design, Sample Size, and Location(s)	Study Population	Key Outcome	ClinicalTrials.gov
Ingavirin	Placebo	Multicentre (8 sites), double-blind Russia N = 240	Outpatient children (6 months-2 years) with influenza and other acute respiratory viral infections	Time to resolution of symptoms	NCT05269290
Onradivir (ZSP1273)	Placebo	Multicentre (76 sites), double-blind China N = 591	Adult outpatients (18 to 64 years) with acute uncomplicated influenza A	Time to alleviation of symptoms	NCT04683406
XC221	Placebo	Multicentre (13 sites), double-blind Russia N = 260	Adult outpatients (18 to 65 years) with uncomplicated influenza or other acute respiratory viral infections	Time to resolution of all symptoms	NCT05544916

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Questions or requests for information about this report can be directed to Requests@CDA-AMC.ca.