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Healthcare resource use and clinical outcomes and experiences with different pre-filled syringes for intravitreal administration of anti-VEGF treatments versus vials: A systematic review protocol

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ADMINISTRATIVE INFORMATION

Support - F. Hoffmann-La Roche Ltd providing funding for third-party writing assistance, which was provided by Luke Carey, PhD, CMPP, of Envision Pharma Group.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - Marloes Bagijn: Employee of F. Hoffmann-La Roche Ltd., Basel, Switzerland. Adam Mapani: Employee of Moorfields Eye Hospital, NHS Foundation Trust, England, UK. Oliver Cox: Employee of F. Hoffmann-La Roche Ltd., Basel, Switzerland. Insaf Saffar: Employee of F. Hoffmann-La Roche Ltd., Basel, Switzerland.

INPLASY registration number: INPLASY202420007

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 02 February 2024 and was last updated on 13 May 2024.

INTRODUCTION

Review question / Objective The aim of this systematic literature review is to assess healthcare resource use outcomes, patient and clinician experiences, and safety associated with the use of different prefilled syringes for intravitreal injection compared with single-use vial-based injection. The proposed systematic review will provide evidence and valuable insights to help guide the development of prefilled syringes for intravitreal injection.

Rationale Treatment of retinal diseases, such as neovascular age-related macular degeneration, diabetic macular edema, and retinal vein occlusion, can require intravitreal injection of single pathway VEGF inhibitors or dual pathway angiopoietin-2/VEGF-A inhibitors. Intravitreal injection may occur subsequent to withdrawal of the medication from a single-use vial using a syringe/needle or by using a syringe prefilled with the medication. The use of prefilled syringes for intravitreal injection is hypothesized to offer a number of advantages for clinicians, nurses, and patients over single-use vial-based injection; however, there has been no systematic evaluation to date comparing outcomes between different anti-VEGF prefilled syringes or comparing outcomes/benefits between anti-VEGF prefilled syringes and single-use vial-based injection administration of anti-VEGF treatments. Our systematic review will evaluate a multitude of patient, clinician, and healthcare system outcomes for these comparisons and will help characterize the impact on the patient-clinician-healthcare system triangle.

Condition being studied The diseases of interest for this systematic review are retinal diseases, including neovascular age-related macular degeneration, diabetic macular edema, and retinal vein occlusion, for which intravitreal injection is indicated and can include injection of single pathway anti-VEGF or dual pathway anti-Ang-2/VEGF-A treatments. Our review will focus on comparing outcomes between various prefilled syringes for intravitreal injection and between prefilled syringes and single-use vial-based injections of these treatments.

METHODS

Search strategy MEDLINE, EMBASE, and The Cochrane Library will be searched combining terms using "OR" within each topic and "AND" between topics.
MEDLINE and The Cochrane Library
1) Prefilled syringe terms
Free text: "prefill", "prefilled", "pre-fill", "pre-filled", "PFS", "ready to administer", "ready to use"

2) Intravitreal injection terms
MeSH: "eye", "injections, intraocular", "intravitreal injections", "vitreous body"
Free-text: "eye", "intraocular", "intravitreal", "ocular", "vitreous"

Search string
(("prefill"[Title/Abstract] OR "prefilled"[Title/Abstract] OR "pre-fill"[Title/Abstract] OR "pre-filled"[Title/Abstract] OR "PFS"[Title/Abstract] OR "ready to administer"[Title/Abstract] OR "ready to use"[Title/Abstract]) AND ("eye"[MeSH Terms] OR "injections, intraocular"[MeSH Terms] OR "intravitreal injections"[MeSH Terms] OR "vitreous body"[MeSH Terms] OR "eye"[Title/Abstract] OR "intraocular"[Title/Abstract] OR "intravitreal"[Title/Abstract] OR "ocular"[Title/Abstract] OR "vitreous"[Title/Abstract])) NOT ("progression free"[Title/Abstract] OR "progression-free"[Title/Abstract] OR "posterior fixation suture*"[Title/Abstract] OR "parafoveal scotoma"[Title/Abstract] OR "postural fluctuation*"[Title/Abstract] OR "postparalytic facial synkinesis"[Title/Abstract] OR "physician fee schedule"[Title/Abstract] OR "parallel fiber*"[Title/Abstract] OR "punctate fluorescein staining"[Title/Abstract] OR "pollen food syndrome"[Title/Abstract] OR "Parkinson* fatigue scale"[Title/Abstract])
EMBASE
1) Prefilled syringe terms
Free text: "prefill", "prefilled", "pre-fill", "pre-filled", "PFS", "ready to administer", "ready to use"
2) Intravitreal injection terms
EMTREE: "eye", "intraocular drug administration", "intravitreal drug administration", "vitreous body"
Free-text: "eye", "intraocular", "intravitreal", "ocular", "vitreous"
Search string
(((prefill or prefilled or pre-fill or pre-filled or pfs or "ready to use" or "ready to administer") AND (eye or intraocular or intravitreal or ocular or vitreous or eye or intraocular drug administration or intravitreal drug administration or vitreous body)) NOT ("progression free" or "progression-free" or "posterior fixation suture*" or "parafoveal scotoma" or "postural fluctuation*" or "postparalytic facial synkinesis" or "physician fee schedule" or "parallel fiber*" or "punctate fluorescein staining" or "pollen food syndrome" or "Parkinson* fatigue scale")).

Participant or population Patients treated with intravitreal injections using prefilled syringes containing single pathway anti-VEGF treatments. Providers preparing and administering the above.

Intervention Prefilled syringes containing the following: ranibizumab, aflibercept, brolucizumab.

Comparator Single-use vials of the following: ranibizumab, aflibercept, brolucizumab.

Study designs to be included The following literature will be considered for inclusion: systematic reviews and meta-analyses, review articles, randomized controlled trials, open-label designs, observational studies (including case series and case reports), time and motion studies, human factor studies, surveys, reports, opinion pieces, and economic analyses.

Eligibility criteria Any literature reporting on the outcomes of interest in patients treated with intravitreal injections using prefilled syringes containing ranibizumab, aflibercept, or brolucizumab, or literature reporting on healthcare providers preparing and administering such injections. Literature reporting results involving off-label compounding or splitting practices will be excluded.

Information sources MEDLINE, EMBASE, and The Cochrane Library will be searched.
Websites from the following organizations will be searched using free-text terms to identify relevant grey literature:
US Food and Drug Administration
European Medicines Association
National Institute for Health and Care Excellence
Scottish Medicines Consortium
Pharmaceutical Benefits Advisory Committee

Canadian Agency for Drugs and Technologies in Health
ISPOR
EconLit Database
American Society of Retinal Specialists
European Society of Retina Specialists
The Association for Research and Vision in Ophthalmology
American Academy of Ophthalmology
The Retina International World Congress of Ophthalmology
The American Macular Degeneration Foundation
The Royal Australian and New Zealand College of Ophthalmologists
Asia-Australia Controversies in Ophthalmology
The Royal College of Ophthalmologists
United Kingdom Ophthalmology Alliance
References lists will be hand searched to identify additional potentially relevant literature.

Main outcome(s) The following outcomes related to procedural efficiency, healthcare resource use, patient and clinician experience, and safety will be evaluated.

Procedural efficiency & healthcare resource use:
Preparation and/or injection time
Preparation and/or injection costs
Preparation and/or injection steps
Precision of intravitreal dosing
Convenience/procedural simplicity
Handling errors or contamination
Wastage (drug or other components)

Supplies used per injection (e.g. needles, syringes)
Effects on staff/clinic management/health system
Cost effectiveness

Patient and clinician experience:
Patient preference or satisfaction
Clinician preference or satisfaction
Patient health-related quality of life

Safety:
Transient vision loss
Increased intraocular pressure
Intraocular inflammation/endophthalmitis
Vitreous floaters
Intraocular air bubbles / silicone oil droplets/ subvisible particles
Treatment discontinuation/withdrawal due to adverse events
Preventable adverse events (associated with handling and administration).

Data management Two reviewers (not authors) will conduct the literature search. After removal of duplicates, each reviewer will screen the records retrieved to determine eligibility. Disagreement will be resolved by discussion among the reviewers and, if necessary, consultation with the authors.
A single reviewer will extract the following data/ information into predefined spreadsheets: general information (authors, publication year, journal), methodological details (design, population, population size, intervention, comparator), and relevant outcomes as listed above.

Quality assessment / Risk of bias analysis Risk of bias will be assessed using the appropriate Joanna Briggs Institute Critical Appraisal Checklist for different types of literature.

Strategy of data synthesis Data will be summarized descriptively; no analyses will be performed.

Subgroup analysis No subgroup analyses will be performed.

Sensitivity analysis No sensitivity analyses will be performed.

Language restriction No language restriction will be imposed.

Country(ies) involved France; Switzerland; United Kingdom.

Keywords Aflibercept; Angiopoietin-2; Brolucizumab; Faricimab; Injection; Intravitreal; Prefilled syringe; Ranibizumab; VEGF.

Dissemination plans The findings of this systematic review will be submitted for publication in a peer-reviewed journal.

Contributions of each author
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