Solstice

MEDICAL PROPELLANT HFO-1234ZE(E), GMP

AN ULTRA-LOW GLOBAL WARMING POTENTIAL (GWP) MEDICAL PROPELLANT FOR METERED DOSE INHALERS

Metered dose inhalers (MDIs) have been in use for more than 65 years. The chlorofluorocarbons (CFCs) used in the first MDIs were replaced with hydrofluoroalkane (HFA) propellants by 2013 in accordance with the Montreal Protocol. However, concerns around the use of HFAs have grown since these compounds can be potent greenhouse gases. In fact, according to the Climate and Clean Air Coalition, phasing down all use of HFAs worldwide can avoid up to 0.5˚ Celsius of global warming by the turn of the century.[1]

Medical Propellant HFO-1234ze(E), GMP uses Hydrofluoroolefin (HFO) technology, a sustainable alternative to HFAs in MDIs. With an ultra-low GWP, HFO-1234ze(E), GMP is a breakthrough medical propellant currently in clinical development for MDIs with the ability to reduce greenhouse gas emissions of propellant by up to 99.9% versus the current inhaler propellant.

HFO-1234ze(E), GMP does not contribute to ground-level ozone creation and is VOC-exempt per the U.S. Environmental Protection Agency (EPA) and the California Air Resource Board (CARB).

A PROVEN SAFETY PROFILE

HFO-1234ze(E), GMP has undergone an extensive battery of toxicology studies that are able to support FDA Investigational New Drug (IND) filings. Pre-clinical toxicology studies include: acute inhalation exposure, repeated dose inhalation exposure, genotoxicity, and reproductive and developmental toxicity in multiple species. Additional long-term repeated dose studies are ongoing in multiple species. In a human clinical study, HFO-1234ze(E), GMP was not found to be a human skin sensitizer. The results of those studies concluded that HFO-1234ze(E), GMP exhibited a good safety profile for its use in Metered Dose Inhalers as well as other potential drug delivery systems.

FLAMMABILITY

HFO-1234ze(E), GMP does not exhibit vapor flame limits under standard test conditions. It is therefore classified as non-flammable according to EC Testing Method A11: Flammability of Gases, and by the U.S. Department of Transportation (DOT) standard (tested according to ASTM E681). HFO-1234ze(E), GMP is non-flammable in the ASTM flame projection test, and it is found to be nonflammable in the ignition distance test and the enclosed space ignition test (closed drum test).[2]

DRUG MASTER FILE

A Drug Master File (DMF) was filed with the U.S. FDA in June 2020 containing information as it pertains to Solstice's manufacturing, quality, toxicology studies, and container closure systems. The DMF has been used to successfully support Phase 1 clinical trials, with Phase 3 clinical trials to commence. Additionally, a DMF has been filed in China (NMPA) and Japan (PMDA). As of June 2026, HFO-1234ze(E), GMP is the world's first LGWP propellant in pMDIs approved for patient use in three countries and a region – UK, EU, AU and NZ.[1] Additional approvals are forthcoming.

REGULATORY COMPLIANCE

As an alternative solution to anticipated HFA phase-down by the Environmental Protection Agency (EPA) and other governing bodies, HFO-1234ze(E), GMP complies with global regulations. It is registered in Europe under REACH (Regulation 1907/2006) for tonnages of more than 1,000 tonnes/annum. Solstice technology has been SNAP listed in various end-use applications since 2010, and is also registered or in compliance with chemical inventories in Japan, China, Canada, Australia, New Zealand, South Korea, Russia, Taiwan, Thailand, and Vietnam.

AVAILABILITY

50-lb and 1,000-lb samples of HFO-1234ze(E), GMP are available for evaluation. Information about commercial quantities is available upon request.

1. AstraZeneca. Trixeo Aerosphere approved in the UK as first inhaled respiratory medicine using next-generation propellant with near-zero Global Warming Potential, May 2025. https://www.astrazeneca.com/media-centre/press-releases/2025/trixeo-aerosphere-approved-in-the-uk-as-first-inhaled-respiratory-medicine-using-next-generation-propellant-with-near-zero-global-warming-potential.html

   AstraZeneca. Trixeo Aerosphere receives positive EU CHMP opinion as first inhaled medicine using next-generation propellant with near-zero Global Warming Potential. https://www.astrazeneca.com/media-centre/press-releases/2025/trixeo-aerosphere-receives-positive-eu-chmp-opinion-first-inhaled-medicine-using-next-generation-propellant-with-near-zero-global-warming-potential.html

   Australian Government Department of Health, Disability and Aging. ARTG ID 475305. https://www.tga.gov.au/resources/artg/475305

   New Zealand Breztri Aerosphere data sheet. https://www.medsafe.govt.nz/profs/datasheet/b/breztriinh.pdf

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PHYSICAL PROPERTIES COMPARED WITH HFA PROPELLANTS*

ATTRIBUTE	HFO-1234ze(E), GMP	HFA-134a	HFA-152a
Global Warming Potential (GWP) vs. CO_2, 100-year ITH[3]	1.37	1530	164
Volatile Organic Compound (VOC)	No	No	No
Flammability[2]	No	No	No
LFL/UFL (Vol. % in Air at 21°C)	None	None	None
Molecular Weighr	114	102	66
Boiling Point (°C)	-19	-26	-25
Vapor Pressure at 70°F/21°C at 130°F/54°C	64.2 PSIA (4.42 bar) 161.7 PSIA (11.15 bar)	85.8 PSIA (5.92 bar) 213.4 PSIA (14.71 bar)	77.0 PSIA (5.31 bar) 190.6 PSIA (13.14 bar)
Specific Gravity at 21°C	1.17	1.22	0.91

* These are just some of a mosaic of properties that must be considered in identifying a suitable propellant.

1. EPA Phasedown of Hydrofluorocarbons
2. Flammability Assessment
3. IPCC Assessment Report 6

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