2.0 Elements for a public summary

2.1 Overview of disease epidemiology

Xylometolazine is indicated to treat the symptoms of nasal congestion associated with rhinitis or sinusitis. Rhinitis is defined as inflammation of the nasal membranes and is typically characterized as any combination of the following symptoms: sneezing, nasal congestion, nasal itching, and rhinorrhea (runny nose). Allergic rhinitis is the most common form of rhinitis. It is an extremely common condition, affecting approximately 20 % (1 in 5) of the population. Non-allergic rhinitis has a number of different causes including infections such as sinusitis, environmental irritants such as cleaning solutions and car exhaust fumes, hormonal imbalances and exposure to certain medications. According to a 2007 Danish study, non-allergic rhinitis affects up to 25 % of the population, and nearly half of these individuals seek treatment for relief of their symptoms [1].

Sinusitis is a condition caused by inflammation of the lining of the paranasal sinuses. Sinusitis rarely occurs without concurrent rhinitis since the nasal membranes are typically also involved. Acute sinusitis affects 3 in 1000 people in the United Kingdom. Chronic sinusitis affects 1 in 1000 people [2]. Sinusitis is more common in winter than in summer.

2.2 Summary of treatment benefits

Xylometolazine is a decongestant nasal spray that works by acting on 'alpha' receptors that are found in the walls of blood vessels in the linings of the nasal passages. It causes these blood vessels to contract and narrow, thereby decreasing blood flow into the linings of the nose and sinuses. This reduces swelling and the feeling of nasal congestion. It also reduces the production of mucus, helping to relieve a blocked nose.

The nasal spray helps relieve congestion in a few minutes (typically 5-10 minutes) and the effect of the medicine lasts for up to 10 hours. As the medicine causes the blood vessels in the nose to contract, it minimises the amount of medicine that is absorbed into the bloodstream from the nose. This means that the nasal spray has a relatively local effect in the nose and thereby reduces the risk of side effects on other parts of the body.

2.3 Unknowns relating to treatment benefits

Not applicable.

2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Rebound nasal congestion following the long-term use of nasal decongestants (Rhinitis medicamentosa)	Long-term use of nasal decongestants beyond the recommended duration of treatment (no longer than 10 days) can lead to rebound congestion of the nasal passages. Patients often try increasing both the dose and the frequency of nasal sprays in an attempt to gain the same symptom relief but this effectively worsens the condition. The condition typically resolves once use of the sprays are stopped altogether.	Yes, by limiting the duration of use and providing clear advice to prescribers and patients in the package insert.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Increased sympathomimetic effects in patients with heart disease, hyperthyroidism, high blood pressure, glaucoma and brain surgery exposing the dura mater.	Sympathomimetic drugs such as xylometolazine are known to have a constrictive effect on blood vessels that can lead to reduced blood flow to the organs and tissues of the body and also lead to an increase in heart rate and blood pressure. It should therefore not be used in patients with known pre-existing cardiovascular conditions associated with poor blood perfusion or elevated blood pressure. Glaucoma occurs when the drainage tubes within the eye become blocked and pressure builds up. Due to the constrictive effect xylometolazine has on blood vessels, it can make the fluid build up in the eye worsen, leading to eventual loss of vision.
Overdose	Sympathomimetic drugs such as xylometolazine mimic the effects of transmitter substances of the sympathetic nervous system such as adrenaline. Common sympathetic effects include sweating and an increase in heart rate and blood pressure. If xylometolazine is used at an excessive dose or taken my mouth then these sympathetic effects can become extreme and lead to increased temperature, palpitations, profuse sweating and eventual cardiovascular collapse and shock.
Drug interaction with tri-cyclic or tetra-cyclic antidepressants or monoamine oxidase inhibitors	If xylometolazine is administered in conjunction with other drugs that act on the sympathetic nervous system, such as antidepressants of the tri-cyclic, tetra-cyclic or monoamine oxidase inhibitor class, then sympathomimetic effects (as listed under Overdose section above) may become exaggerated and potentially harmful. Xylometolazine use is therefore not recommended in patients concurrently using these medications.
Increased blood glucose in diabetic patients	Drug such as xylometolazine, that exert effects on the sympathetic nervous system, are known to suppress insulin secretion (the hormone that controls blood glucose levels) and thereby can cause a rebound increase in blood glucose levels. This effect can be exacerbated in diabetic patients who already have impaired glucose control mechanisms. Therefore, use in diabetic patients is not recommended.

Important missing information

Risk	What is known
Pregnancy and breast-feeding	There is limited human experience with xylometolazine use during pregnancy and breast-feeding. For this reason its use is not recommended during pregnancy due to the unknown potential risks to the developing fetus. Patients are advised to consult with their physician if intending to use the drug while breast-feeding as it is unknown whether xylometolazine enters the breast milk.
Off-label use in infants and toddlers	Xylometolazine efficacy and safety has not been established in infants and toddlers and should therefore not be used in children under 2 years old due to the risk of overdose. It should also not be used during pregnancy due to the potential vasoconstrictive effect on the placental blood supply and fetal exposure.

2.5 Summary of additional risk minimisation measures by safety concern

Not applicable.

2.6 Planned post authorisation development plan (if applicable)

Not applicable.

2.7 Summary of changes to the risk management plan over time

Not applicable.