

## Supplementary Information

**Article Title:** Adverse Drug Reactions of Intranasal Corticosteroids in the Netherlands: An Analysis from the Netherlands Pharmacovigilance Center.

**Journal name:** Drugs - Real World Outcomes

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Table 1: Overview of reported ADRs on HLT level

ADR (HLT name)	Includes (PT name)	Reports
Nasal disorders NEC	Epistaxis Nasal crusting; Nasal disorder; Nasal dryness; Nasal mucosal disorder; Nasal oedema; Nasal polyps; Nasal pruritus; Nasal septum perforation	159
Headaches NEC	Headache; Sinus headache	145
Upper respiratory tract signs and symptoms	Aphonia; Dry throat; Dysphonia; Nasal discomfort; Oropharyngeal discomfort; Oropharyngeal pain; Rhinalgia; Rhinorrhoea; Sneezing; Throat irritation; Throat tightness; Yawning	105
Olfactory nerve disorders	Anosmia; Hyposmia; Parosmia	95
Sensory abnormalities NEC	Ageusia; Dysgeusia; Hypogeusia; Sensory disturbance; Taste disorder	78
Neurological signs and symptoms NEC	Dizziness; Head discomfort; Presyncope	70
Breathing abnormalities	Dyspnoea; Dyspnoea exertional; Hyperventilation; Respiratory distress	60
Therapeutic and nontherapeutic responses	Adverse event; Drug ineffective; Drug intolerance; Therapeutic product effect decreased; Therapeutic product effect incomplete; Therapeutic product ineffective; Therapeutic response decreased; Therapeutic response unexpected	60
Cardiac signs and symptoms NEC	Palpitations	52
Rashes, eruptions and exanthems NEC	Rash; Rash erythematous; Rash macular; Rash pruritic; Rash vesicular	46
Asthenic conditions	Asthenia; Fatigue; Malaise	44
Nausea and vomiting symptoms	Nausea; Retching; Vomiting	43
Upper respiratory tract infections	Nasal abscess; Nasopharyngitis; Pharyngitis; Rhinitis; Sinusitis; Tonsillitis; Upper respiratory tract infection	35
Anxiety symptoms	Agitation; Anxiety; Nervousness; Stress; Tension	32
General signs and symptoms NEC	Condition aggravated; Crying; Exercise tolerance decreased; Illness; Influenza like illness; Peripheral swelling; Secretion discharge; Swelling; Swelling face	29
Visual disorders NEC	Diplopia; Photopsia; Vision blurred	28
Disturbances in consciousness NEC	Loss of consciousness; Somnolence; Stupor; Syncope	25
Pain and discomfort NEC	Chest discomfort; Chest pain; Discomfort; Facial pain; Pain	25
Visual impairment and blindness (excl colour blindness)	Blindness; Visual acuity reduced; Visual impairment	24
Coughing and associated symptoms	Cough; Haemoptysis; Productive cough; Sputum increased	23
Feelings and sensations NEC	Chills; Feeling abnormal; Feeling cold; Feeling hot; Feeling jittery; Feeling of body temperature change; Hunger; Sensation of foreign body; Sense of oppression	23
Inner ear signs and symptoms	Tinnitus; Vertigo	23
Ocular disorders NEC	Eye disorder; Eye pain; Eye swelling; Lens disorder; Ocular discomfort; Periorbital oedema	23
Pruritus NEC	Pruritus	23
Paraesthesias and dysaesthesias	Burning sensation; Burning sensation mucosal; Hyperaesthesia; Hypoaesthesia; Paraesthesia	22
Nasal congestion and inflammations	Nasal congestion	20
Disturbances in initiating and maintaining sleep	Initial insomnia; Insomnia	19
Migraine headaches	Migraine; Migraine with aura; Migraine without aura	19
Bronchospasm and obstruction	Asthma; Bronchospasm; Chronic obstructive pulmonary disease; Wheezing	18
Ocular infections, inflammations and associated manifestations	Eye inflammation; Eye irritation; Ocular hyperaemia	17
Tongue signs and symptoms	Glossodynia; Swollen tongue; Tongue blistering; Tongue discolouration; Tongue erythema; Tongue oedema	17
Interactions	Drug interaction; Food interaction; Inhibitory drug interaction	16
Urticarias	Urticaria	16
Gastrointestinal and abdominal pains (excl oral and throat)	Abdominal pain; Abdominal pain upper	15
Rate and rhythm disorders NEC	Arrhythmia; Extrasystoles; Tachycardia	14
Allergic conditions NEC	Hypersensitivity	13
Cataract conditions	Cataract; Cataract subcapsular	13
Haemorrhages NEC	Haematoma; Haemorrhage	13
Dermatitis and eczema	Dermatitis; Dermatitis allergic; Dermatitis contact; Eczema; Perioral dermatitis	12
Eye and eyelid infections	Conjunctivitis; Eye infection; Hordeolum; Retinitis	12
Muscle pains	Myalgia	12
Oral soft tissue signs and symptoms	Hypoaesthesia oral; Odynophagia; Oral discomfort; Oral mucosal blistering; Oral pain; Paraesthesia oral	12
Angioedemas	Angioedema	11
Apocrine and eccrine gland disorders	Hyperhidrosis; Night sweats	11
Dermal and epidermal conditions NEC	Papule; Scab; Skin burning sensation; Skin disorder; Skin odour	11

	abnormal; Skin reaction; Skin warm	
Diarrhoea (excl infective)	Diarrhoea	11
Erythemas	Erythema	11
Lacrimation disorders	Dry eye; Lacrimation disorder; Lacrimation increased	11
Menstruation and uterine bleeding NEC	Menstrual disorder; Menstruation irregular; Metrorrhagia	11
Mood alterations with depressive symptoms	Depressed mood; Feeling of despair; Negative thoughts; Tearfulness	11
Oedema NEC	Face oedema; Oedema peripheral	11
Parasomnias	Abnormal dreams; Nightmare; Parasomnia; Somnambulism	11
Product quality issues NEC	Product complaint; Product quality issue; Product substitution issue	11
Appetite disorders	Appetite disorder; Decreased appetite	10
Alopecias	Alopecia; Alopecia areata	9
Dyspeptic signs and symptoms	Dyspepsia; Eructation	9
Ear disorders NEC	Ear congestion; Ear discomfort; Ear pain	9
Gastrointestinal signs and symptoms NEC	Abdominal discomfort; Breath odour; Dysphagia	9
Glaucomas (excl congenital)	Glaucoma; Ocular hypertension	9
Muscle related signs and symptoms NEC	Muscle mass; Muscle spasms; Myokymia	9
Oral dryness and saliva altered	Dry mouth; Saliva altered; Salivary hypersecretion	9
Pharyngeal disorders (excl infections and neoplasms)	Pharyngeal hypoaesthesia; Pharyngeal swelling; Tonsillar disorder	9
Physical examination procedures and organ system status	Body temperature decreased; Weight decreased; Weight increased	9
Application and instillation site reactions	Application site burn; Application site reaction	8
Candida infections	Candida infection; Oesophageal candidiasis; Oral candidiasis	8
Ophthalmic function diagnostic procedures	Intraocular pressure increased	8
Panic attacks and disorders	Panic attack; Panic reaction	8
Adrenal cortical hyperfunctions	Cushing's syndrome; Cushingoid	7
Dyskinesias and movement disorders NEC	Psychomotor hyperactivity	7
Heart rate and pulse investigations	Heart rate decreased; Heart rate increased; Heart rate irregular	7
Joint related signs and symptoms	Arthralgia; Joint stiffness	7
Medication errors, product use errors and issues NEC	Device difficult to use; Product use complaint; Product use in unapproved indication; Product use issue; Wrong technique in product usage process	7
Memory loss (excl dementia)	Memory impairment	7
Mental impairment (excl dementia and memory loss)	Disturbance in attention; Mental impairment	7
Oral soft tissue swelling and oedema	Lip swelling; Oedema mouth; Palatal swelling	7
Choroid and vitreous structural change, deposit and degeneration	Chorioretinopathy; Vitreous detachment; Vitreous floaters	6
Emotional and mood disturbances NEC	Anger; Euphoric mood; Irritability	6
Hearing losses	Deafness; Hypoacusis	6
Hypertrichoses	Hirsutism; Hypertrichosis	6
Musculoskeletal and connective tissue pain and discomfort	Back pain; Neck pain; Pain in extremity	6
Purpura and related conditions	Ecchymosis; Petechiae; Purpura	6
Tongue disorders	Glossitis; Tongue disorder	6
Tremor (excl congenital)	Tremor	6
Adrenal cortical hypofunctions	Adrenal insufficiency; Adrenal suppression; Secondary adrenocortical insufficiency	5
Bullous conditions	Blister; Dermatitis bullous; Pemphigus	5
Coordination and balance disturbances	Balance disorder	5
Exposures associated with pregnancy, delivery and lactation	Exposure during pregnancy; Foetal exposure during pregnancy; Maternal exposure during pregnancy	5
Febrile disorders	Pyrexia	5
Flatulence, bloating and distension	Abdominal distension; Flatulence	5
Fungal infections NEC	Fungal infection; Fungal oesophagitis; Tongue fungal infection; Vulvovaginal mycotic infection	5
Lid, lash and lacrimal infections, irritations and inflammations	Eyelid irritation; Eyelid oedema; Swelling of eyelid	5
Lower respiratory tract signs and symptoms	Bronchial irritation; Hiccups; Increased bronchial secretion	5
Musculoskeletal and connective tissue conditions NEC	Growth retardation	5
Peripheral vascular disorders NEC	Flushing; Hot flush; Peripheral vascular disorder	5
Product physical issues	Product odour abnormal; Product taste abnormal	5
Skin hypoplasias and atrophies	Skin atrophy; Skin striae	5
Vascular hypertensive disorders NEC	Hypertension	5
Allergies to foods, food additives, drugs and other chemicals	Drug hypersensitivity Reaction to excipient	4
Anaphylactic and anaphylactoid responses	Anaphylactic reaction	4

	Anaphylactic shock	
Bone related signs and symptoms	Pain in jaw	4
Carbohydrate tolerance analyses (incl diabetes)	Blood glucose abnormal; Blood glucose increased	4
Fluctuating mood symptoms	Mood swings	4
Herpes viral infections	Herpes simplex; Herpes zoster; Varicella	4
Increased physical activity levels	Restlessness	4
Mucosal findings abnormal	Mucosal disorder; Mucosal inflammation; Oedema mucosal	4
Muscle weakness conditions	Muscular weakness	4
Ocular bleeding and vascular disorders NEC	Eye haemorrhage	4
Off label uses	Off label use	4
Oral soft tissue disorders NEC	Cheilitis; Oral disorder	4
Sleep disturbances NEC	Poor quality sleep	4
Supraventricular arrhythmias	Atrial fibrillation; Sinus bradycardia	4
Vascular tests NEC (incl blood pressure)	Blood pressure decreased; Blood pressure increased	4
Abortions not specified as induced or spontaneous	Abortion	3
Acnes	Acne; Dermatitis acneiform	3
Adjustment disorders	Adjustment disorder with depressed mood	3
Behaviour and socialisation disturbances	Aggression	3
Bladder and urethral symptoms	Dysuria; Micturition disorder; Urinary incontinence	3
Confusion and disorientation	Confusional state	3
Dental surface disorders	Tooth discolouration	3
Depressive disorders	Depression	3
Erection and ejaculation conditions and disorders	Erectile dysfunction	3
Exfoliative conditions	Exfoliative rash; Skin exfoliation	3
Faecal abnormalities NEC	Abnormal faeces; Faeces hard; Faeces soft	3
Gastrointestinal atonic and hypomotility disorders NEC	Constipation; Gastroesophageal reflux disease	3
Hyperacusia	Hyperacusis	3
Inflammations	Granuloma; Inflammation	3
Lower respiratory tract and lung infections	Bronchitis; Lower respiratory tract infection; Pneumonia	3
Lymphatic system disorders NEC	Lymphadenopathy	3
Menstruation with decreased bleeding	Amenorrhoea	3
Metabolic bone disorders	Osteopenia; Osteoporosis	3
Mood alterations with manic symptoms	Hypomania	3
Ocular sensation disorders	Asthenopia; Photophobia	3
Paranasal sinus disorders (excl infections and neoplasms)	Sinus congestion; Sinus disorder	3
Product administration errors and issues	Incorrect dose administered; Incorrect dose administered by device; Product administration error	3
Psychiatric elimination disorders	Enuresis	3
Pupil disorders	Mydriasis	3
Retinal structural change, deposit and degeneration	Macular degeneration; Retinal degeneration; Retinal detachment	3
Seizures and seizure disorders NEC	Epilepsy; Seizure	3
Stomatitis and ulceration	Aphthous ulcer; Mouth ulceration; Stomatitis	3
Tendon disorders	Tendon disorder; Tendon pain	3
Vulvovaginal disorders NEC	Vaginal haemorrhage	3
Adrenal cortex tests	Cortisol decreased; Glucocorticoids increased	2
Breast disorders NEC	Gynaecomastia	2
Breast signs and symptoms	Breast pain; Nipple swelling	2
Cardiac valve disorders NEC	Cardiac valve disease	2
Central nervous system haemorrhages and cerebrovascular accidents	Cerebral infarction	2
Coagulation and bleeding analyses	Bleeding time prolonged; International normalised ratio fluctuation	2
Cognitive and attention disorders and disturbances NEC	Daydreaming	2
Conjunctival and corneal bleeding and vascular disorders	Conjunctival haemorrhage	2
Dental pain and sensation disorders	Toothache	2
Device issues NEC	Device issue	2
Device malfunction events NEC	Device malfunction; Device occlusion	2
Hepatocellular damage and hepatitis NEC	Liver injury	2
Hyperglycaemic conditions NEC	Hyperglycaemia	2
Immunodeficiency disorders NEC	Immunodeficiency; Immunosuppression	2
Influenza viral infections	Influenza	2

Lactation disorders	Lactation disorder; Suppressed lactation	2
Nail and nail bed conditions (excl infections and infestations)	Nail bed inflammation; Onychoclasia	2
Neuromuscular disorders NEC	Muscle contractions involuntary	2
Oesophagitis (excl infective)	Oesophagitis	2
Paralysis and paresis (excl cranial nerve)	Hemiparesis	2
Pilar disorders NEC	Hair colour changes; Hair growth abnormal	2
Product supply and availability issues	Product availability issue	2
Renal failure and impairment	Acute kidney injury; Renal impairment	2
Respiratory tract disorders NEC	Lung disorder; Respiratory tract irritation	2
Retinal bleeding and vascular disorders (excl retinopathy)	Retinal haemorrhage; Retinal vein thrombosis	2
Site specific vascular disorders NEC	Pallor	2
Skin structures and soft tissue infections	Folliculitis Pyoderma	2
Sleep disorders NEC	Sleep disorder	2
Speech and language abnormalities	Speech disorder	2
Stillbirth and foetal death	Foetal death	2
Suicidal and self-injurious behaviour	Suicidal ideation	2
Therapeutic procedures NEC	Therapy cessation	2
Withdrawal and rebound effects	Drug withdrawal syndrome	2
Accidental exposures to product	Accidental exposure to product	1
Acute and chronic pancreatitis	Pancreatitis acute	1
Affect alterations NEC	Affect lability	1
Arthropathies NEC	Arthropathy	1
Attention deficit and disruptive behaviour disorders	Attention deficit hyperactivity disorder	1
Autosomal chromosomal abnormalities	Trisomy 21	1
Cardiac disorders congenital NEC	Heart disease congenital	1
Cardiac disorders NEC	Cardiac disorder	1
Central nervous system and spinal infections	Brain abscess	1
Cholestasis and jaundice	Cholestasis	1
Circulatory collapse and shock	Shock	1
Colitis (excl infective)	Colitis ulcerative	1
Conditions associated with abnormal gas exchange	Asphyxia	1
Corneal structural change, deposit and degeneration	Corneal perforation	1
Death and sudden death	Death	1
Delusional symptoms	Delusion	1
Dental and periodontal infections and inflammations	Dental caries	1
Device operational issues NEC	Device operational issue	1
Diabetes mellitus (incl subtypes)	Steroid diabetes	1
Ear infections	Otitis media	1
Eating disorders NEC	Binge eating	1
Eustachian tube disorders	Eustachian tube patulous	1
Eye complications associated with device	Eye complication associated with device	1
Eyelid movement disorders	Excessive eye blinking	1
Facial cranial nerve disorders	Facial paralysis	1
Female reproductive tract infections	Vaginal infection	1
Foetal growth complications	Foetal growth restriction	1
Gait disturbances	Gait disturbance	1
Gastric ulcers and perforation	Gastric ulcer	1
Gastrointestinal disorders NEC	Gastrointestinal disorder	1
Gastrointestinal mucosal dystrophies and secretion disorders	Gastrointestinal tract mucosal discolouration	1
Gastrointestinal spastic and hypermotility disorders	Oesophageal spasm	1
General nutritional disorders NEC	Obesity	1
Gingival disorders, signs and symptoms NEC	Gingival pain	1
Hallucinations (excl sleep-related)	Hallucination	1
Impulse control disorders	Impulsive behaviour	1
Infections NEC	Respiratory tract infection	1
Iris and uveal tract infections, irritations and inflammations	Iridocyclitis	1
Ischaemic coronary artery disorders	Arteriospasm coronary	1
Laryngeal and adjacent sites disorders NEC	Laryngeal disorder	1

(excl infections and neoplasms)		
Laryngeal spasm, oedema and obstruction	Laryngotracheal oedema	1
Limb fractures and dislocations	Hip fracture	1
Marrow depression and hypoplastic anaemias	Pancytopenia	1
Mass conditions NEC	Mass	1
Mental disorders NEC	Mental disorder	1
Middle ear disorders NEC	Middle ear disorder	1
Mood disorders NEC	Affective disorder	1
Motor neurone diseases	Motor neurone disease	1
Muscle tone abnormal	Serotonin syndrome	1
Muscle, tendon and ligament injuries	Tendon rupture	1
Musculoskeletal and connective tissue disorders of limbs congenital	Congenital hand malformation	1
Myopathies	Myopathy	1
Neurologic visual problems NEC	Visual field defect	1
Neutropenias	Neutropenia	1
Non-site specific gastrointestinal haemorrhages	Upper gastrointestinal haemorrhage	1
Peripheral neuropathies NEC	Polyneuropathy	1
Photosensitivity and photodermatitis conditions	Photosensitivity reaction	1
Psychiatric symptoms NEC	Psychiatric symptom	1
Reproductive tract signs and symptoms NEC	Pruritus genital	1
Respiratory tract and thoracic histopathology procedures	Sputum abnormal	1
Retinopathies NEC	Retinopathy	1
Sebaceous gland disorders	Seborrhoea	1
Skin haemorrhages	Skin haemorrhage	1
Skin injuries NEC	Contusion	1
Skin vasculitides	Hypersensitivity vasculitis	1
Speech articulation and rhythm disturbances	Dysphemia	1
Spermatogenesis and semen disorders	Azoospermia	1
Staphylococcal infections	Furuncle	1
Stereotypies and automatisms	Bruxism	1
Testicular and epididymal disorders NEC	Testicular pain	1
Tic disorders	Tic	1
Tissue enzyme analyses NEC	Blood alkaline phosphatase increased	1
Total fluid volume increased	Fluid retention	1
Trigeminal disorders	Trigeminal neuralgia	1
Ulcers NEC	Ulcer	1
Unintended pregnancies	Unintended pregnancy	1
Urinary abnormalities	Haematuria	1
Vagus nerve disorders	Vocal cord paralysis	1
Vascular hypotensive disorders	Orthostatic hypotension	1
<b>Abbreviations</b>		
ADR, adverse drug reaction		
HLT, High Level Term NAME OF MedDRA [12]		
NEC, Not elsewhere classified is a standard abbreviation used to denote groupings of miscellaneous terms that do not readily fit into other hierarchical classifications within a particular SOC [12]		
PTname, Preferred Term name of MedDRA [12]		
SOC, System Organ Class level of MedDRA [12]		