PROFESSIONAL INFORMATION

SCHEDULING STATUS

S1

1 NAME OF THE MEDICINE
TRINFLEM 200 mg effervescent tablet.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each effervescent tablet contains 200 mg of acetylcysteine.
Contains sweetener: Saccharin sodium 20,0 mg.
For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Effervescent tablet.
White to off white round, flat effervescent tablet.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
Acetylcysteine is used as a mucolytic in non-infective secretions of patients with respiratory conditions and in cystic fibrosis.

4.2 Posology and method of administration
Posology
Do not use continuously for more than 14 days without consulting a doctor.

Adults and adolescents from 14 years of age:
Take one tablet two to three times a day (equivalent to 400 to 600 mg N- acetylcysteine/day).

Paediatric population
Children from 2 to 5 years of age: ½ effervescent tablet 2 to 3 times daily (equivalent to 200 to 300 mg N-acetylcysteine/day).
Children from 6 to 14 years of age: One tablet twice daily (equivalent to 400 mg N-acetylcysteine/day).

Method of administration
Tablet must be dissolved in a glass of water. The solution should be drunk immediately.

4.3 Contraindications
Hypersensitivity to acetylcysteine or to any of the excipients (see section 6.1).
Pregnancy and lactation (see section 4.6).
Children under 2 years of age.

4.4 Special warnings and precautions for use
Acetylcysteine may cause bronchospasms to occur. If bronchospasm does occur, TRINFLEM should be discontinued immediately. Asthmatic patients and elderly patients with respiratory insufficiency should take caution with [PRODUCT NAME].
Patients with a history of peptic ulcer should use TRINFLEM with caution as it may affect the mucous membrane of the gastrointestinal tract.
Toxic epidermal necrolysis and Stevens-Johnson syndrome have been reported with the use of [PRODUCT NAME]. Immediate medical advice is required if mucosal or cutaneous alterations occur, and the treatment with TRINFLEM should be discontinued immediately.
At the start of the treatment with acetylcysteine, bronchial secretions may become more fluid and increase in volume. Postural drainage and bronchoaspiration should be performed when a patient is unable to cough up the secretions effectively.
TRINFLEM should be used with caution in the long-term treatment of patients with histamine intolerance, as acetylcysteine may slightly affect the metabolism of histamine. Symptoms of intolerance like: headache, vasomotor rhinitis and itching may occur.
A mild sulphurous smell is not indicative of product alterations but is a characteristic of the active ingredient contained in this preparation.

Paediatric population
Due to the physiological characteristics of the airways in children under 2 years of age, mucolytic medicines may obstruct the airways as the ability to cough may be limited (see section 4.3).

4.5 Interaction with other medicines and other forms of interaction
Nitroglycerin's vasodilatory effects may be enhanced by [PRODUCT NAME].
Antitussive medicines should not be used concomitantly with TRINFLEM as congestion of secretions may occur as a result of the impaired cough reflex.
Activated charcoal reduces the absorption of TRINFLEM which will decrease its effect.
If tetracycline hydrochloride (with the exception of doxycycline) and other oral antibiotics are required, it is advised that these should be taken two hours before or after [PRODUCT NAME]; due to the fact that in-vitro tests have reported the inactivation of antibiotics if the products are directly mixed with each other.
Simultaneous solution of TRINFLEM with any other medicinal products is not recommended.
Interactions with laboratory tests
Colorimetric analysis: Acetylcysteine may have an effect on the values of salicylates.

Fertility, pregnancy and lactation
Pregnancy
Safety and/or efficacy in pregnancy has not been established. TRINFLEM is contraindicated during pregnancy (see section 4.3).

Breastfeeding
It is not known whether acetylcysteine or its metabolites passes into human milk.
Safety and /or efficacy in lactation has not been established. Mothers on TRINFLEM should not breastfeed their babies (see section 4.3).

Fertility
There are no indications for possible effects of the use of acetylcysteine on fertility.

4.7 Effects on ability to drive and use machines
TRINFLEM should have no effect on the ability to drive.

4.8 Undesirable effects
Tabulated summary of adverse reactions

MedDRA system organ class	Frequency	Adverse reactions
Immune system disorders	Less frequent	Hypersensitivity, allergic reactions (pruritis, urticarial, exanthema, rash, bronchospasm, angioedema, tachycardia, hypotension and hypertension), anaphylactic shock, anaphylactic reactions, Stevens-Johnson syndrome, toxic epidermal necrolysis (see section 4.4)
Nervous system disorders	Less frequent	Headache
	Frequency unknown	Syncope, convulsions
Eye disorders	Less frequent	Blurred vision
Ear and labyrinth disorders	Less frequent	Tinnitus
Cardiac disorders	Frequency unknown	Cardiac arrest
Vascular disorders	Less frequent	Haemorrhages
	Frequency unknown	Flushing, sweating
Respiratory, thoracic and mediastinal disorders	Less frequent	Rhinorrhoea, bronchospasm, dyspnoea
	Frequency unknown	Haemoptysis, respiratory arrest
Gastrointestinal disorders	Less frequent	Vomiting, nausea, stomatitis, abdominal pain, diarrhoea, dyspepsia, heartburn
Hepato-biliary disorders	Frequency unknown	Disturbances of liver function
Skin and subcutaneous tissue disorders	Less frequent	Urticaria
	Frequency unknown	Facial oedema
Musculoskeletal and connective tissue disorders	Frequency unknown	Arthralgia
General disorders and administration site conditions	Less frequent	Pyrexia, chills
Investigations	Less frequent	Low blood pressure
	Frequency unknown	Acidosis

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:
https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose -
Overdoses may lead to gastrointestinal effects such as vomiting, diarrhoea and nausea.
Treatment will be symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
N-acetylcysteine is a mucolytic medicine that reduces the viscosity of non-infected bronchial secretions probably by the splitting of disulphide bonds in mucoproteins.

5.2 Pharmacokinetic properties
Absorption
Acetylcysteine is almost completely and rapidly absorbed, following oral administration. The bioavailability of orally administered acetylcysteine is very low (approx. 10 %) due to the high first pass effect.

Distribution
The liver, lungs and kidney receive the highest tissue concentration.

Biotransformation
The liver rapidly metabolises acetylcysteine in the liver to cysteine, which is the pharmacologically active metabolite. It is also metabolised to diacetylcysteine and further mixed disulphides.

Elimination
Renal clearance is approximately around 30 % of the total body clearance.
The terminal half-life of total acetylcysteine is 6,25 (4,59 – 10,6) hours, following oral administration. High doses are excreted by the kidneys as it is largely converted to inactive metabolites like inorganic sulfate.

Linearity/non-linearity
The pharmacokinetics of acetylcysteine is dose proportional in the dose range of 200 - 3200 mg/m^2 for C_{max} and AUC.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Maltodextrin
Citric acid anhydrous
Sodium hydrogen carbonate
Saccharin sodium
Orange Flavour
Leucine

6.2 Incompatibilities
Acetylcysteine can react with metal (e.g., iron, nickel, copper) and rubber. Use of glass and/or plastic delivery systems is recommended when administering via nasointestinal or nasogastric tube. Do not mix acetylcysteine and antibiotics prior to administration.

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Considering that an effervescent product is sensitive to moisture the tube should be closed tightly and not stored near moisture.

6.5 Nature and contents of container
20 tablets in a polypropylene tube closed with a polyethylene stoppers equipped with silica gel as drying agent.

6.6 Special precautions for disposal
No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION
Trinity Pharma
106 16th Road
Midrand
1686

8 REGISTRATION NUMBER
TRINFLEM : 48/10.2.2/0469

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
22 June 2021

10 DATE OF REVISION OF THE TEXT
N.A

TRINITY PHARMA

Tel: 010 594 5610. Email: PV@kahmagroup.co.za

PROFESSIONELE INLIGTING

SKEDULERINGSTATUS

S1

1 NAAM VAN DIE GENEESMIDDEL
TRINFLEM 200 mg bruistablet.

2 KWALITATIEWE EN KWANTITATIEWE SAMESTELLING
Elke bruistablet bevat 200 mg asetielsisteïen.
Bevat versoeter: natriumsakkarien 20,0 mg
Sien afdeling 6.1 vir 'n volledige lys van die onaktiewe bestanddele.

3 FARMASEUTIESE VORM
Bruistablet.
Wit tot spierwit ronde, plat bruistablet.

4 KLINIESE BESONDERHEDE
4.1 Terapeutiese indikasies
Asetielsisteïen word gebruik as 'n mukolitiese middel tydens nie-besmette afskeidings in pasiënte met respiratoriese toestande asook pasiënte met sistiese fibrose.

4.2 Dosering en metode van toediening
Dosis
Moet nie langer as 14 dae aaneenlopend gebruik sonder om 'n dokter te raadpleeg nie.

Volwassenes en adolessente vanaf 14 jaar:
Neem een tablet twee tot drie keer per dag (gelykstaande aan 400 tot 600 mg N-asetielsisteïen / dag).

Pediatriese populasie
Kinders van 2 tot 5 jaar: ½ bruistablet 2 tot 3 keer per dag (gelykstaande aan 200 tot 300 mg N-asetielsisteïen / dag).
Kinders van 6 tot 14 jaar oud: Een tablet twee keer per dag (gelykstaande aan 400 mg N-asetielsisteïen / dag).

Metode van toediening
Die tablet moet in 'n glas water opgelos word. Die oplossing moet onmiddellik gedrink word.

4.3 Kontra-indikasies
Hipersensitiwiteit vir asetielsisteïen of vir enige van die onaktiewe bestanddele (sien afdeling 6.1).
Swangerskap en laktasie (sien afdeling 4.6).
Kinders jonger as 2 jaar.

4.4 Spesiale waarskuwings en voorsorgmaatreëls vir gebruik
Asetielsisteïen kan brongospasma tot gevolg hê. Indien brongospasma voorkom, moet TRINFLEM onmiddellik gestaak word. Asmatiese pasiënte en bejaarde pasiënte met respiratoriese inkorting moet TRINFLEM met omsigtigheid gebruik.
Pasiënte met 'n geskiedenis van peptiese ulkusse moet TRINFLEM met omsigtigheid gebruik, aangesien dit die slymvlies van die spysverteringskanaal kan affekteer.
Giftige epidermale nekrolise en Stevens-Johnson-sindroom is gerapporteer met die gebruik van [PRODUKNAAM]. Onmiddellike mediese advies is nodig indien slymvlies- of kutane veranderinge voorkom en die behandeling met TRINFLEM moet onmiddellik gestaak word.
Aanvangsbehandeling met asetielsisteïen kan brongiale afskeidings vermeerder asook meer vloeibaar maak. Posturale dreinering en brongo-aspirasie moet uitgevoer word indien die pasiënt nie die afskeidings effektief kan uithoes nie.
TRINFLEM moet met omsigtigheid gebruik word tydens langtermynbehandeling in pasiënte met histamienintoleransie, aangesien asetielsisteïen die metabolisme van histamien effens kan beïnvloed. Simptome van onverdraagsaamheid soos: hoofpyn, vasomotoriese rinitis en jeuk kan voorkom.
'n Ligte, swaelagtige reuk is nie 'n aanduiding van produkafbraak nie, maar is kenmerk aan die aktiewe bestanddeel wat in hierdie produk voorkom.

Pediatriese populasie
As gevolg van die fisiologiese eienskappe van die lugweë by kinders jonger as 2 jaar, kan mukolitiese medisyne die lugweë belemmer, aangesien die vermoë om te hoes ingeperk kan word (sien afdeling 4.3).

4.5 Interaksie met ander medisyne en ander vorme van interaksie
Die vasodilaterende effekte van nitrogliserien kan verhoog word deur [PRODUKNAAM].
Hoesonderdrukkers moet nie saam met TRINFLEM gebruik word nie, aangesien verstopping as gevolg van afskeidings en verswakte hoesrefleks kan voorkom.
Geaktiveerde houtskool verminder die opname van [PRODUKNAAM], wat die effek daarvan sal verminder.
Indien tetrasiklienhidrochloried (met die uitsondering van doksisiklien) en ander orale antibiotika benodig word, word dit aanbeveel dat dit twee uur voor of na TRINFLEM geneem moet word. In-vitro-toetse het getoon dat antibiotika geïnaktiveer word indien die produkte met mekaar gemeng word.
Gelyktydige oplossing van TRINFLEM met enige ander medisyne word nie aanbeveel nie.
Interaksies met laboratoriumtoetse
Kolorimetriese analise: Asetielsisteïen kan die vlakke van salisilate beïnvloed.

Vrugbaarheid, swangerskap en laktasie
Swangerskap
Veiligheid en/of doeltreffendheid tydens swangerskap is nog nie vasgestel nie. TRINFLEM is teenaangedui tydens swangerskap (sien afdeling 4.3).

Borsvoeding
Dit is nie bekend indien asetielsisteïen of die metaboliete daarvan in menslike melk uitgeskei word nie.
Veiligheid en/of effektiwiteit tydens borsvoeding is nog nie vasgestel nie. Moeders wat TRINFLEM neem moet nie hul babas borsvoed nie (sien afdeling 4.3).

Vrugbaarheid
Daar is geen aanduidings vir die moontlike effekte op vrugbaarheid tydens die gebruik van asetielsisteïen nie.

4.7 Effekte op die vermoë om te bestuur en masjiene te gebruik
TRINFLEM behoort geen invloed te hê op die vermoë om te bestuur nie.

4.8 Ongewenste effekte
Opsomming van ongewenste effekte in tabelvorm

MedDRA orgaansisteem klassifikasie	Frekwensie	Nadelige reaksies
Immuunstelselafwykings	Minder gereeld	Hipersensitiwiteit, allergiese reaksies (pruritis, urtikarie, eksantem, uitslag, brongospasma, angio-edeem, tagikardie, hipotensie en hipertensie), anafilaktiese skok, anafilaktiese reaksies, Stevens-Johnson-sindroom, toksiese epidermale nekrolise (sien afdeling 4.4)
Senuweestelselafwykings	Minder gereeld	Hoofpyn
	Frekwensie onbekend	Sinkopie, stuiptrekkings
Oogafwykings	Minder gereeld	Dowwe sig
Oor- en labirintafwykings	Minder gereeld	Tinnitus
Hartafwykings	Frekwensie onbekend	Hartaanval
Vaskulêre afwykings	Minder gereeld	Bloedings
	Frekwensie onbekend	Gloede, sweet
Asemhalings-, torakale en mediastinumafwykings	Minder gereeld	Rinoree, brongospasma, dispnee
	Frekwensie onbekend	Hemoptise, asemhalingsaanval
Gastro-intestinale afwykings	Minder gereeld	Braking, naarheid, stomatitis, buikpyn, diarree, dispepsie, sooibrand
Hepato-bilière afwykings	Frekwensie onbekend	Versteurings in lewerfunksie
Vel- en subkutaneuse weefselafwykings	Minder gereeld	Urtikarie
	Frekwensie onbekend	Edeem van die gesig
Spier- en bindweefselafwykings	Frekwensie onbekend	Artralgie
Algemene afwykings en toedieningsplektoestande	Minder gereeld	Pyreksie, kouekoors
Ondersoeke	Minder gereeld	Lae bloeddruk
	Frekwensie onbekend	Asidose

Aanmelding van vermeende newe-reaksies
Die aanmelding van vermoedelike nadelige reaksies na goedkeuring van hierdie medisyne is belangrik. Dit laat voortgesette monitering van die voordeel/risikobalans van die medisyne toe. Verskaffers van gesondheidsorg word gevra om enige vermeende nadelige reaksies aan SAHPRA te rapporteer via die "6.04 Adverse Drug Reactions Reporting Form", wat aanlyn onder SAHPRA se publikasies voorkom:
https://www.sahpra.org.za/Publications/Index/8

Oordosis
Oordosering kan lei tot gastro-intestinale effekte soos braking, diarree en naarheid.
Behandeling moet simptomaties en ondersteunend wees.

5 FARMAKOLOGIESE EIENDOMME
5.1 Farmakodinamiese eienskappe
N-asetielsisteïen is 'n mukolitiese middel wat die viskositeit van nie-besmette brongiale afskeidings verminder, moontlik deur die breking van disulfiedbindings in mukoproteïen.

5.2 Farmakokinetiese eienskappe
Absorpsie
Asetielsisteïen word vinnig en byna volledig geabsorbeer na orale toediening. Die biobeskikbaarheid van oraal toegediende asetielsisteïen is baie laag (ongeveer 10 %) as gevolg van die hoë eerste deurgangseffek.

Verspreiding
Die hoogste weefselkonsentrasies word gevind in die lewer, longe en niere.

Biotransformasie
Die lewer metaboliseer asetielsisteïen vinnig na sisteïen, wat die farmakologiese aktiewe metaboliet is. Dit word ook gemetaboliseer tot diasetielsisteïen en ander gemengde disulfiede.

Uitskeiding
Nieruitskeiding vorm ongeveer 30 % van die totale liggaamsuitskeiding.
Die terminale halfleeftyd van totale asetielsisteïen is 6,25 (4,59 – 10,6) uur na orale toediening. Hoë dosisse word deur die niere uitgeskei, aangesien dit hoofsaaklik in onaktiewe metaboliete soos anorganiese sulfaat omgeskakel word.

Lineêr / Nie-lineêr
Die farmakokinetika van asetielsisteïen is dosisproporsioneel oor die dosiswydte van 200 – 3200 mg / m^2 vir K_{maks} en AOK.

6 FARMASEUTIESE BESONDERHEDE
6.1 Lys van onaktiewe bestanddele
Maltodekstrien
Watervrye sitroensuur
Natriumwaterstofkarbonaat
Natriumsakkarien
Lemoengeursel
Leusien

6.2 Onversoenbaarheid
Asetielsisteïen kan reageer met metale (bv. yster, nikkel, koper) en rubber. Die gebruik van glas- en/of plastiektoedieningstelsels word aanbeveel wanneer dit deur middel van die neus of 'n neusbuis toegedien word. Moet nie asetielsisteïen met antibiotika meng voor toediening nie.

6.3 Rakleeftyd
3 jaar.

6.4 Spesiale voorsorgmaatreëls vir bewaring
Aangesien 'n bruisende produk sensitief is vir vog, moet die buis dig toegemaak word en nie in die teenwoordigheid van vog gebêre word nie.

6.5 Aard en inhoud van die houer
20 tablette in 'n polipropileenbuis, toegemaak met 'n poliëtileenprop met silikajel as droogmiddel.

6.6 Spesiale voorsorgmaatreëls vir wegdoening
Geen spesiale vereistes word benodig nie. Ongebruikte medisyne of afvalmateriaal moet in ooreenstemming met die plaaslike vereistes weggegooi word.

7 HOUER VAN SERTIFIKAAT VAN REGISTRASIE
Trinity Pharma
16de Weg 106
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1686

8 REGISTRASIENOMMERS
TRINFLEM : 48/10.2.2/0469

9 DATUM VAN EERSTE MAGTIGING / HERNUWING VAN DIE MAGTIGING
22 Junie 2021

10 DATUM VAN HERSIENING VAN DIE TEKS
N.A