יוני 2026

Actilyse 20 mg	Actilyse 50 mg
אקטיליז 20 מ"ג	**אקטיליז 50 מ"ג**
alteplase 20 mg/vial	**alteplase 50 mg/vial**
powder and solvent for solution for injection/infusion	**powder and solvent for solution for injection/infusion**

הנדון: עדכון עלון לצרכן במתכונת עלון לרופא

רופא/ה יקר/ה, רוקח/ת יקר/ה,

חברת בורינגר אינגלהיים ישראל בע"מ מבקשת להודיעכם על עדכון בעלון לצרכן במתכונת עלון לרופא של התכשירים שבנדון.

ההתוויות הרשומות לתכשירים בישראל:

Acute myocardial infarction:
Actilyse is indicated for use in the management of acute myocardial infraction (AMI) in adults for the lysis of thrombi obstructing coronary arteries, the reduction of infract size, improvement of ventricular function, the reduction of the incidence of congestive heart failure and the reduction of mortality associated with AMI.
Treatment should be initiated as soon as possible after the onset of AMI symptoms.

Acute massive pulmonary embolism with hemodynamic deprivation:
Actylise is indicated in the management of acute massive pulmonary embolism (PE) in adults:
- for the lysis of acute pulmonary emboli, defined as obstruction of blood flow to a lobe or multiple segments of the lung, and
- for the lysis of pulmonary emboli accompanied by unstable hemodynamics e.g. failure to maintain blood pressure without supportive measures.
The diagnosis should be confirmed by objective means, such as pulmonary angiography or noninvasive procedures such as lung scanning.

For fibrinolytic treatment of acute ischaemic stroke:
Treatment must be started as early as possible within 4.5 hours after onset of stroke symptoms and after exclusion of intracranial haemorrhage by appropriate imaging techniques (e.g. cranial computerized tomography or other diagnostic imaging method sensitive for the presence of haemorrhage). The treatment effect is time-dependent; therefore earlier treatment increases the probability of a favourable outcome. This treatment is restricted to a prescription by a specialist in neurology.

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השינויים המשמעותיים ביותר בעלון סומנו מטה כדלקמן:
טקסט עם קו תחתי בכחול מציין טקסט שהוסף לעלון.
טקסט עם קו חוצה מציין טקסט שהוסר מן העלון.

למידע נוסף יש לעיין בעלון לצרכן במתכונת עלון לרופא המאושר.
העלון המעודכן נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות.
כמו כן, ניתן לקבלו על-ידי פנייה לבעל הרישום:
בורינגר אינגלהיים ישראל בע"מ, רח' מדינת היהודים 89 הרצליה פיתוח, ובטלפון 09-9730500

בברכה,

בורינגר אינגלהיים ישראל

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

…
Excipient(s) with known effect
Each 20 mg vial contains 2.0 mg polysorbate 80 (E 433).
Each 50 mg vial contains 5.0 mg polysorbate 80 (E 433).
…

4.3 Contraindications

Hypersensitivity to the active substance alteplase, gentamicin (a trace residue from the manufacturing process) or to any of the excipients listed in section 6.1.

Contraindications in acute myocardial infarction, acute massive pulmonary embolism and acute ischaemic stroke:

Actilyse is contraindicated in ~~cases where there is~~ situations associated with a high risk of ~~haemorrhage~~ bleeding such as:

- significant bleeding disorder at present or within the past 6 months
- known haemorrhagic diathesis
- ~~patients receiving effective oral anticoagulant treatment (e.g. warfarin sodium with INR >1.3) (see section 4.4)~~
- manifest or recent severe or dangerous bleeding
- ~~known history of or suspected intracranial haemorrhage~~
- ~~suspected subarachnoid haemorrhage or condition after subarachnoid haemorrhage from aneurysm~~
- any history of central nervous system damage (i.e. neoplasm, aneurysm, intracranial or spinal surgery)
- recent (less than 10 days) ~~traumatic external heart massage,~~ obstetrical delivery, recent puncture of a non-compressible blood-vessel (e.g. subclavian or jugular vein puncture)
- severe uncontrolled arterial hypertension (see section 4.4)
- bacterial endocarditis, pericarditis
- acute pancreatitis

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- ~~documented~~active ulcerative gastrointestinal disease~~ during the last 3 months~~, oesophageal varices, known arterial-aneurysm~~,~~ and/or arterial/venous ~~malformations~~malformation
  - neoplasm with increased bleeding risk
  - severe liver disease, including hepatic failure, cirrhosis, portal hypertension (oesophageal varices) and active hepatitis
  - major surgery or significant trauma in past 3 months.

Additional contraindications in acute myocardial infarction~~:~~

- ~~any known history of haemorrhagic stroke or stroke of unknown origin .~~
- ~~known history of ischaemic stroke or transient ischaemic attack (TIA) in the preceding 6 months, except current acute ischaemic stroke within 4.5 hours.~~

~~Additional contraindications in~~ and acute massive pulmonary embolism:

- any known history of haemorrhagic stroke or stroke of unknown origin~~.~~
- known history of ischaemic stroke or transient ischaemic attack (TIA) in the preceding 6- months~~,~~ except current acute ischaemic stroke within 4.5 hours.
- patients receiving effective oral anticoagulant treatment (e.g. vitamin K antagonists with INR > 1.3) (see section 4.4).

Additional contraindications in acute ischaemic stroke:

- symptoms of ischaemic attack beginning more than 4.5 hours prior to infusion start or symptoms for which the onset time is unknown and could potentially be more than 4.5 hours ago (see section 5.1)
- minor neurological deficit or symptoms rapidly improving before start of infusion
- severe stroke as assessed clinically (e.g. NIHSS>25) and/or by appropriate imaging techniques
- ~~seizure at onset of stroke~~
- known history of or suspected intracranial haemorrhage
- evidence of intracranial haemorrhage (ICH) on the CT-scan
- symptoms suggestive of subarachnoid haemorrhage, even if CT-scan is normal
- patients receiving effective anticoagulation (e.g. vitamin K antagonists with INR > 1. 7) (see section 4.4)
- administration of heparin within the previous 48 hours and a thromboplastin time exceeding the upper limit of normal for laboratory
- patients with any history of prior stroke and concomitant diabetes
- prior stroke within the last 3 months
- platelet count of below 100~~,~~ 000/mm^3
- systolic blood pressure > 185 mm Hg or diastolic BP > 110 mm Hg, or ~~aggressive management (intravenous pharmacotherapy) necessary to reduce~~when BP ~~to~~cannot be reduced below these limits by careful management
- blood glucose < 50 mg/~~dl~~dL (see section 4.4) or > 400 mg/~~dl (<~~dL (< 2.~~8mM~~8 mM or > 22.~~2mM~~2 mM).

Use in children and adolescents

Actilyse is not indicated for the treatment of acute ischaemic stroke in children under 16 years of age (for adolescents ≥ 16 years of age see section 4.4).

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4.4- Special warnings and precautions for use

…

~~Haemorrhages~~ Bleeding

…

~~As with all thrombolytic agents, the~~The expected therapeutic benefit should be weighed up particularly carefully against the possible risk, especially in patients with

- small recent traumas, such as biopsies, puncture of major vessels, intramuscular injections~~,~~ ~~cardiac massage for resuscitation~~
- ~~conditions with an increased risk of haemorrhage which are not mentioned in section 4.3.~~

- ~~Patients~~prolonged (> 2 minutes) or traumatic cardiopulmonary resuscitation or cardiac massage
- patients receiving oral anticoagulant treatment: The use of Actilyse may be considered when dosing or time since the last intake of anticoagulant treatment makes residual efficacy unlikely confirmed by appropriate test(s) of anticoagulant activity for the product(s) concerned showing no clinically relevant activity on the coagulation system (e.g. INR≤ 1.3 (AMI and PE) or INR ≤ 1.7 (AIS) for vitamin K antagonists or other relevant test(s) for other oral anticoagulants are within the respective upper limit of normal).

Thrombo-embolism

The use of Actilyse can increase the risk of thrombo-embolic events in patients with existing thrombi, e.g., left heart thrombus (mitral stenosis or atrial fibrillation, etc.).

…

The expected therapeutic benefit should be weighed up particularly carefully against the possible risk, especially in patients with~~-~~:

- systolic blood pressure > 160 mm Hg (see section 4.3) ~~and with~~
- body weight < 50 kg
- advanced age, i.e. patients 75 years or older, which may increase the risk of intracerebral haemorrhage. ~~As the therapeutic benefit is also positive in elderly patients, the risk-benefit-evaluation should be carried out carefully.~~

…

~~Thromboembolism:~~

~~The use of thrombolytics can increase the risk of thrombo-embolic events in patients with left heart thrombus, e.g., mitral stenosis or atrial fibrillation.~~

Additional special warnings and precautions in acute ischaemic stroke:

~~Special precautions for use:~~

Thrombolytic treatment requires adequate monitoring. Treatment must ~~only~~ be performed under the responsibility and follow-up of a physician trained and experienced in neurovascular care~~.~~ and the use of thrombolytic treatments, with the facilities to monitor that use. For the verification of treatment indication remote diagnostic measures may be considered as appropriate ~~(~~see section 4.1~~).~~ and 4.2.

Special warnings / conditions with a decreased benefit/risk ratio:

Bleeding

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Intracerebral haemorrhage represents the major adverse reaction in the treatment of acute ischaemic stroke (up to 15 % of patients without any increase of overall mortality and without any relevant increase in overall mortality and severe disability combined, i.e. modified Rankin scale [mRS] score of 5 and 6).
Compared to other indications~~,~~ patients with acute ischaemic stroke treated with Actilyse have a markedly increased risk of intracranial haemorrhage as the bleeding occurs predominantly into the infarcted area. This applies in particular in the following cases:

- ~~all situations listed in section 4.3. and in general all situations involving a high risk of haemorrhage~~
- as time to treatment from onset of stroke symptoms increases, net clinical benefit decreases. Therefore, the administration of Actilyse should not be delayed.
- patients pre-treated with ~~acetyl salicylic~~acetylsalicylic acid (ASA) may have a greater risk of intracerebral haemorrhage and/or mortality, particularly if Actilyse treatment is delayed.
- ~~Compared~~compared to younger patients, patients of advanced age (over 80 years) may have a somewhat poorer outcome independent of treatment. They are also more likely to have more severe strokes which are associated with a higher absolute risk of intracerebral haemorrhage when thrombolysed compared with milder strokes when thrombolysed or with non-thrombolysed patients. Although available data indicate that the net benefit of Actilyse in patients over 80 years is smaller compared with younger patients, Actilyse can be used in patients over 80 years on an individual benefit-risk basis (see section 5.1). Patients of advanced age should be selected very carefully taking into account both the general health and the neurological status.

Special groups at reduced benefit/risk ratio
The benefit/risk ratio of Actilyse administration should be thoroughly considered in AIS patients with the following conditions:

- the therapeutic benefit is reduced in patients that had a prior stroke (see also section 4.3) or in those with known uncontrolled diabetes, thus the benefit/risk ratio is considered less favourable, but still positive in these patients~~.~~
- ~~In~~in patients with very mild stroke, the risks outweigh the expected benefit (see section 4.3)
- ~~Patients~~patients with very severe stroke are at higher risk for intracerebral haemorrhage and death and should not be treated (see section 4.3)
- ~~Patients~~patients with extensive infarctions are at greater risk of poor outcome including severe haemorrhage and death. In such patients, the benefit/risk ratio should be thoroughly considered~~.~~
- ~~In~~in stroke patients the likelihood of good outcomes decreases with longer time to treatment from onset of symptoms, increasing age, increasing stroke severity and increased levels of blood glucose on admission while the likelihood of severe disability and death or symptomatic intracranial bleedings increases, independently from treatment~~.~~
- seizure at the onset of stroke (Thrombolytic therapy in these patients should only be considered when there is no suspicion of a stroke mimic or significant head trauma)~~.~~
- in patients initially presenting with blood glucose < 50 mg/dL, thrombolysis may be considered after correction to normal blood glucose values, if the diagnosis of AIS persists (see section 4.3).

…
Actilyse contains polysorbate 80
This medicine contains 2.0 mg or 5.0 mg of polysorbate 80 in each 20 mg or 50 mg vial, respectively. Polysorbates may cause allergic reactions.

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4.5 Interaction with other medicinal products and other forms of interaction

No formal interaction studies with Actilyse and medicinal products commonly administered in patients with acute myocardial infarction, acute massive pulmonary embolism or acute ischaemic stroke have been performed.

Drugs affecting coagulation/platelet function

~~The risk of haemorrhage is increased if coumarine derivatives, oral anticoagulants, platelet aggregation inhibitors, unfractionated heparin or LMWH or active substances which interfere with~~ Medicinal products that affect coagulation ~~are~~or those that alter platelet function may increase the risk of bleeding (when administered ~~(before~~prior to, during or ~~within~~after alteplase therapy). These products should be avoided in the first 24 hours after Actilyse treatment ~~with Actilyse) (~~for acute ischaemic stroke. With regard to pre-treatment with these substances, see sections 4.2, 4.3, and 4.~~3).~~4.

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