

Summary of Product Characteristics/SPC
TRH FERRING 0. 2 mg/ml solution for injection

1. Name of the medicinal product

TRH FERRING 0. 2 mg/ml solution for injection

2. Qualitative and quantitative Composition

1 ampoule with 1 ml solution for injection contains 0. 2 mg protirelin (thyrotropin-releasing Hormone).
Complete list of other components, see section 6. 1.

3. Pharmaceutical form

Solution for injection

4. Clinical data

4. 1 Fields of application

Protirelin is used to carry out implementation of the TRH test as part of the diagnosis of the thyroid gland and pituitary gland.

4. 2 Posology, Type and duration of application

Dosage

Adults: 1 – 2 1/2 ampoules of TRH (each ampoule contains 200 µg of protirelin). In adults, the usual dose is of 200 µg for diagnostic purposes is enough.

Children from 2 weeks of age the dose is 1 microgram of protirelin/kg body weight.

Very little data is available in newborns younger than 2 weeks of age. Data have been published on dosing from 7 to 20 µg/kg bw.

Type and duration of application

For a single i.v. injection as a diagnostic agent. If the test is repeated, a time interval of 14 days should be observed.

Intravenous TRH test:

After taking approx. 5 ml of venous blood to determine the serum basal value of TSH becomes TRH FERRING slowly (via at least 1 minute) injected intravenously.

After about 30 minutes, another 5 ml of blood is added for the second determination of the serum TSH levels.

In children with suspected congenital hypothyroidism an additional sample is required after 180 minutes.

Evaluation of the TRH test:

The statement of the TRH test results from the difference between the stimulated value and the basal value for TSH (= Δ TSH). Check table above

Because of the circadian rhythm of TSH blood levels, baseline and comparative values should be recorded between 9 a.m. and 5 p.m., as no significant fluctuations in TSH blood concentrations are expected during this time.

As the thyrotropin suppressive therapy carried out, the Protirelin test allows only after several weeks therapy-free interval, a statement about thyroid function.

Functional position of the thyroid gland	TSH Mirror μ U/ml	TSH to TRH μ U/ml	Δ TSH μ U/ml
1. Euthyroidism	≤ 4 normal	≤ 25 Increase	$\geq 2 < 25$
2. Hyperthyroidism	< 4 low	< 4 no increase	< 2
3. primary hypothyroidism	> 4 increased	> 25 sharp increase	≥ 25
4. Sec. (HVL) hypothyroidism	unverifiable	no increase	-

Under treatment with levothyroxine and/or liothyronine, a 24-hours pause should be observed if a protirelin test is carried out in conjunction with a determination of thyroid hormone constituent concentration in the serum is provided.

4. 3 Contraindications

TRH FERRING must not be used in the case of:

- Hypersensitivity to the active substance or one of the listed in (section 6. 1) excipients
- acute heart attack
- unstable angina pectoris
- increased readiness to cramp
- pronounced bronchial obstruction

4. 4 Special warnings and precautions for use

TRH FERRING should only be used after careful balancing consideration of the risk-benefit

- arrhythmias
- ischemic heart disease
- poorly adjusted hypertension
- large pituitary tumors
- Epilepsy
- Bronchial asthma

Following thyrostatic treatment of hyperthyroidism, a pathological protirelin test may be present for a long time.

To avoid misinterpretations in case of thyroid function, the correct application of Protirelin in the intravenous test and the observance of the time interval for the determination of the stimulating thyrotropin value are required.

TRH FERRING contains sodium, but less than 1 mmol (23 mg) of sodium per ampoule.

5. Interactions with others Pharmaceuticals and other Interactions

Levothyroxine, dextrothyroxine and liothyronine, as well as other thyroid hormone analogs, such as triiodothyroacetic acid, dose-dependently inhibit the thyrotropin increase in the protirelin test. The increase is reduced by glucocorticoids, somatostatin, dopamine, bromocriptin, lisuride, levodopa, salicylates, morphine, barbiturates and X-ray contrast agents.

It is intensified, above all usually only weakly, by simultaneous administration of GnRH, GHRH, CRH, estrogens, clomiphene, spironolactone, iodide, amiodarone, lithium, theophylline, metoclopramide, domperidone, sulpiride, chlorpromazine, biperiden, haloperidol or prostaglandins.

However, the significance of the test can only be influenced by these interactions in very rare cases.

4. 6 Fertility, pregnancy and Breastfeeding

The use of Protirelin is generally not necessary during pregnancy and lactation

Pregnancy

Protirelin crosses the placenta and stimulates the release of thyrotropin, T₃, T₄ and prolactin. The data on the use of TRH in pregnant women is inadequate.

Animal studies have shown reproductive toxicity (see section 5.3). The potential risk to humans is not known

Breastfeeding

It is not known whether protirelin/metabolites are excreted in human milk. Side effects in breastfed infants are not known.

Fertility

No data are available on the effects of Protirelin on fertility.

4.7 Effects on the ability to drive operating machinery.

Not applicable.

4. 8 Undesirable effects

When TRH Ferring is administered intravenously, short-term (over 1 – 3 minutes) is to be expected with a feeling of heat, nausea, urge to urinate, mild headache, drowsiness, flushing, Abnormal sensations in the area of the abdominal and pelvic organs.

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As with any IV injection of peptides, an anaphylactic reaction cannot be ruled out.

In individual patients with large pituitary tumors, acute local complications due to enlargement of the tumor or apoplexy of the pituitary gland (headache, impaired consciousness, cranial nerve paralysis, visual

impairment up to amaurosis, hemiplegia), some of which required neurosurgical interventions. TRH was there in most cases, has been administered in the form of a combined pituitary gland test together with other substances.

It is not clear whether the complications can be attributed to TRH only.

Reporting of suspected adverse reactions after authorisation is of great importance. It enables continuous monitoring of the risk-benefit of the drug.

Members of Health professionals are called to inform upon to suspected case of side effect the Federal Institute for Drugs and medical devices

Pharmacovigilance Dept.

Kurt-Georg-Kiesinger-Allee 3

D-53175 Bonn

Website: www.bfarm.de

MedDRA System Organ Class	Uncommon (0.1 – 1%)	Rare (0.01 – 0.1%)
Diseases of the Nervous system	Lack of taste Fertilizations	Convulsions in predisposed patients*
Vascular diseases	Increase in blood pressure, increase in pulse	Asthma in predisposed Patients**
diseases of the respiratory system, of the thoracic cavity and mediastinum	Abnormal sensations in of the chest	
Diseases of the Gastrointestinal tract	Dry mouth, vomiting	
Skeletal muscle- Connective tissue and Disorders	Abnormal sensations in the Extremities	
Diseases of the kidneys and urinary tract		
Diseases of the genital organs and of the mammary gland		
General disorders and complaints on Place of administration	tightness in the chest, Hunger	

* Triggering of a seizure in case of increased convulsive readiness

** Triggering an asthma attack in asthmatics

4.9 Overdose

No cases of overdose have been reported. In case of overdose, the reported side effects may occur (see section 4.8). Since Protirelin is fastly eliminated from the body, there is no need to take any measures in case of overdose.

5. Pharmacological properties

5.1 Pharmacodynamic properties Pharmacotherapeutic group:

Thyroid function tests, Protirelin

ATC code: V04C J02

TRH, which is effective on the pituitary gland, is formed in the hypothalamus and passes through the portal vein circulation to the anterior pituitary gland. There it leads to the release of thyrotropin with a subsequent increase in serum thyrotropin levels and increased thyrotropin resynthesis.

In healthy people, TRH leads at the same time as a prolactin secretion from the pituitary gland, in prolactinoma, this stimulation is attenuated or absent. In contrast, a TRH-induced release of growth hormone (STH, GH) is only evident in acromegaly.

5.2 Pharmacokinetic properties:

Maximum serum levels for Protirelin can be expected after 2 – 5 minutes after intravenous administration. Accordingly, the maximum thyrotropin levels are found after 20 – 30 minutes.

The tripeptide protirelin is rapidly enzymatically degraded in serum and tissues. The serum half-life is approximately 3 – 6.5 minutes, with both native protirelin and metabolites excreted in the urine.

5.3 Preclinical data on safety

Acute toxicity

Studies on the acute toxicity of protirelin are not available.

Chronic toxicity

Chronic toxicity studies of the protirelin are not present.

Mutagenic and tumorigenic potential

Protirelin has not been adequately studied regarding mutagenic effects.

A bacterial test for gene mutation results negative.

There are no long-term studies on animals of a potential tumor-generating

Reproductive toxicity

Protirelin crosses the placenta. Protirelin increased the number of resorptions in the rabbit at 1.5 times the human dose. No effects were observed in the rat at up to 6 times the human dose.

Investigations on mice and rabbits found no evidence of a teratogenic potential of protirelin. Prenatal protirelin exposure accelerated, especially associated with glucocorticoids, the fetal lung maturation, the "alveolar air expansion index" is significantly increased and the survival time of premature infants after a single dose of Protirelin is higher than in control animals (lamb, rabbit).

6. Pharmaceutical particulars

6. 1 List of excipients

Sodium chloride, water for injections, hydrochloric acid 10 %.

6. 2 Incompatibilities

None. Since there are no compatibility studies this product must not be mixed with other medicinal products

6. 3 Shelf life

4 years

6. 4 Special precautions for storage

Do not store above 25°C.

6. 5 Type and contents of the container

TRH FERRING 0.2 mg/ml solution for injection is provided as a single 1 ml dose in colorless glass ampoules (type I).

Surgery with 1 ampoule of 1 ml solution for injection

Surgery with 5 ampoules, each containing 1 ml solution for injection

6.6 Special precautions for disposal and other instructions for handling

6. 6 Special precautions

Any unused medicinal product or waste material must be classified in accordance with national requirements to be disposed

7. Marketing authorisation holder

FERRING GmbH

Wittland 11

D-24109 Kiel

Co-distributors

FERRING Arzneimittel GmbH

Factory road 7

D-24103 Kiel

Tel. 0431-5852-0

Tel. 0431-5852-74

8. Approval number

6079289. 00. 00

9. Date of issue of marketing authorisation/

Renewal of marketing authorisation

01. 09. 1998/04. 08. 2015

10. State of information

August 2015

11. Sales demarcation

Prescription-only If you have any further questions
Please contact us at the following e-mail address:
info-service@ferring.de