SUMMARY OF PRODUCT CHARACTERISTICS
ADIONE® 10mg / 10mg

1. NAME OF THE MEDICINAL PRODUCT:

ADIONE® 10mg / 10mg (Doxylamine Succinate / Pyridoxine Hydrochloride), delayed release coated enteric tablets.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each coated enteric tablet contains as active ingredients:

- Doxylamine succinate 10 mg
- Pyridoxine Hydrochloride 10mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Enteric coated tablets with delayed release.

4. CLINICAL DATA

4.1 Therapeutic indications

ADIONE®10mg / 10mg is indicated for the management of nausea and vomiting of pregnancy.

4.2 Posology and method of administration

Oral way

Initially, take two ADIONE® Oral Release Tablets at bedtime (Day 1). If this dose adequately controls the symptoms the next day, continue taking two tablets daily at bedtime. However, if symptoms persist in the afternoon of Day 2, take the usual dose of two tablets at bedtime that night and then take three tablets from Day 3 (one tablet in the morning and two tablets in the evening at bedtime). If this dose adequately controls symptoms on Day 4, continue taking three tablets daily. Otherwise take four tablets from Day 4 (one tablet in the morning, one tablet in the middle of the afternoon and two tablets in the evening at bedtime). The maximum recommended dose is four tablets (one tablet in the morning, one tablet in the middle of the afternoon and two tablets in the evening at bedtime) per day.

The maximum recommended dose is 4 tablets daily (one tablet in the morning, one tablet mid-afternoon and two tablets at bedtime).The length of treatment depends on the persistence of the symptoms and with doctor consent. Security and efficacy of ADIONE® ´s tablets for children less than 18 years have not been established.

POSOLOGY	Overall number of tablets per day	Number of tablet(s)		
		Morning	Mid-afternoon	Bedtime
Day 1	2	0	0	2
Day 2	2	0	0	2
If at day 2 the symptoms are controlled, continue taking 2 tablets at bedtime. If symptoms persist at mid-afternoon of day 2, take 3 tablets starting at day 3.				
Day 3	3	1	0	2
If at day 3 the symptoms are controlled, continue taking 1 tablet in the morning and 2 tablets at bedtime. If symptoms persist at day 4, take 4 tablets starting at day 4.				
Day 4 and next days	4	1	1	2

The safety and effectiveness of ADIONE® tablets in children under 18 years of age have not been established

4.3. Contraindications

ADIONE® is contraindicated in women with known hypersensitivity to:

- Doxylamine succinate
- Pyridoxine Hydrochloride
- Has other antihistamines derived from ethanolamine
- Any inactive ingredient in the formulation

ADIONE® is contraindicated in women who are taking Monoamine Oxidase (MAO) Inhibitors.

4.4. Special warnings and precautions for use

ADIONE® use is not recommended if a woman is concurrently using Central Nervous System (CNS) depressants including alcohol. The combination may result in severe drowsiness leading to falls or accidents.

ADIONE® has anticholinergic properties and, therefore, should be used with caution in women with: asthma, increased intraocular pressure, narrow angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction and urinary bladder-neck obstruction.

4.5 Interactions with other drugs and other forms of interaction

Doxylamine Succinate may enhance the sedative effect of CNS depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives

and antipsychotics. There is an increased risk of antimuscarinic side effects when Doxylamine is given with other antimuscarinic drugs.

Pyridoxine reduces the effect of levodopa.

4.6 Pregnancy and lactation

ADIONE® is intended for use in pregnant women, the reference product of ADIONE® has been classified as Category A by FDA (Food and Drug Administration).

The molecular weight of Doxylamine Succinate is low enough that passage into breast milk can be expected. Women should not breastfeed while using ADIONE®.

4.7 Effects on ability to drive and use machines

ADIONE® influence on the ability to drive and use machines. This medicine may cause drowsiness, especially during the first days of administration.

4.8 Undesirable effects

The most common adverse reaction associated with Doxylamine Succinate is somnolence. Other adverse drug reactions associated with Doxylamine Succinate may include: vertigo, nervousness, epigastric pain, headache, palpitation, diarrhea, disorientation, irritability, convulsions, urinary retention or insomnia.

Pyridoxine is a vitamin that is generally recognized as having no adverse effects.

4.9 Overdose

For Doxylamine, overdose phenomena have been described at doses of 250 to 1000 mg per day. Symptoms of overdose with an antihistamine include agitation, mydriasis, and accommodation paralysis, dryness of the mouth, flushing of the face and neck, hyperthermia and sinus tachycardia. Acute intoxication with doxylamine is sometimes responsible for rhabdomyolysis, which can be complicated by acute renal failure.

Pyridoxine is associated with side effects only after long-term use of high doses. Severe neuropathy has been reported in patients receiving high doses of pyridoxine (2 to 6 g daily).

Treatment includes gastric lavage, emetics, universal antidote, and respiratory stimulants.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Doxylamine Succinate is an antihistamine, which diminishes or abolishes the major actions of histamine in the body by competitive, reversible, blockade of histamine receptor sites on tissues. It is a sedative antihistamine and has a market anti-emetic activity. Hence can be used to control nausea and vomiting. Nausea in the first trimester of pregnancy does not require drug therapy, but on rare occasions, if vomiting is severe an antihistamine such as Doxylamine may be used. Pyridoxine, a water-soluble vitamin belonging to the B-complex group has been shown to be safe and effective in the treatment of nausea and vomiting of pregnancy. Although the exact mechanism of action of pyridoxine is not known, well-controlled clinical trials have shown pyridoxine to reduce the severity of nausea and the episodes of vomiting associated with the early pregnancy.

5.2 Pharmacokinetic properties

ADIONE® tablets have a delayed action formulation with an optimal effect when taken 4 to 6 hours before the presumed time of symptom onset. The maximum concentrations for Doxylamine succinate and pyridoxine are reached in 7.5 and 5.5 hours, respectively. Doxylamine succinate is absorbed in the gastrointestinal system. The terminal half-life of doxylamine elimination is 12.5 hours. Pyridoxine is readily absorbed from the gastrointestinal tract following oral administration and converted to the active forms, pyridoxal phosphate and Pyridoxamine phosphate. They are stored in the liver wherein there is oxidation to 4-pyridoxic acid and other interactive metabolites which are excreted in the urine. As the dose increases the greater amounts are excreted unchanged in the urine. Pyridoxal crosses the placenta and also appears in the breast milk.

5.3 Preclinical safety data:

Not applicable

6. PHARMACEUTICAL DATA

6.1 List of excipients

Colloidal Anhydrous silica, Magnesium Trisilicate, Microcrystalline cellulose, Croscarmellose sodium, Magnesium Stearate, Hypromellose, Purified Talc, Macrogol 400, Titanium Dioxide, Dichloromethane, Methacrylic Acid and Methyl Methacrylate Copolymer (1:1), Acetone, Macrogol 6000, Purified Water, Isopropyl alcohol and Ferric oxide red.

6.2 Incompatibilities

Doxylamine Succinate may enhance the sedative effect of CNS depressants including alcohol, barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives

and antipsychotics. There is an increased risk of antimuscarinic side effects when Doxylamine is given with other antimuscarinic drugs.

Pyridoxine reduces the effect of levodopa.

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store ADIONE® at a temperature below 30 ºC in a dry environment away from light.

Keep out of sight and reach of children.

6.5 Nature and contents of the outer packaging:
ADIONE® is supplied in blister packs of 10 tablets (containing 1 blister Aluminum / Aluminum) or 30 tablets (containing 3 blisters Aluminum / Aluminum of 10 tablets).

6.6 Special precautions for disposal and handling
No special requirements

7. MARKETING AUTHORIZATION HOLDER

CROSS PHARM S.A.
Quai des Bergues, 23
1201 Geneve - Switzerland

8. MARKETING AUTHORIZATION NUMBER (CIP Code)
Not applicable

9. DATE OF FIRST AITORIZATION / RENEWAL OF AUTHORIZATION
(To be completed by the holder after granting the AMM)

10. DATE OF REVISION OF THE TEXT
06/2019

11. DOSIMETRY
Not applicable

12. INSTRUCTIONS FOR THE PREPARATION OF RADIOPHARMACEUTICALS
Not applicable