ڤالساتينس أقراص مغلفة

فالسارتان ٤٠ مجم ،٨٠ مجم

تحذير

لا يستخدم اثناء الحمل حيث انه قد يسبب اصابة او وفاة الجنين.

معلومات للمرضى

ينصح المريض بقراءة النشرة المعتمدة (معلومات للمريض)

يجب قراءة النشرة المرفقة مع **فالساتينس** قبل تناول هذا الدواء وعند تكراره قد تضاف معلومات جديدة. هذه النشرة ليست بديلا عن طبيبك عند حدوث اعراض طبية او العلاج.

إذا كان لديك أي أسئلة عن **فالساتينس**، اسال طبيبك او الصيدلي.

ماهي المعلومات الهامة جدا التي يجب ان اعرفها عن فالساتينس؟

فالساتينس يمكن ان يسبب ضرر او وفاة للطفل اثناء الحمل. تكلم مع طبيبك عن الاساليب الأخرى لحفظ ضغط الدم إذا كنت تخططين للحمل. إذا كنت حاملا وتتناولين **فالساتينس**، اسال طبيبك علي الفور .

ما هو فالساتينس؟

يصرف **فالساتينس** عن طريق روشتة الطبيب و يسمى مثبطات مستقبلات انجيوتنسين ٢. يستخدم مع البالغين ل:

- تقليل ضغط الدم المرتفع (ارتفاع الضغط) في البالغين والأطفال من عمر ٦ الى ١٦ سنة.
- لعلاج فشل عضلة القلب في البالغين في هؤلاء المرضى، **فالساتينس** قد يقلل من الاحتياج لدخول المستشفى الذي يحدث من فشل عضلة القلب.
- يحسن من فرص الحياة أطول بعد حدوث الازمة القلبية (جلطة بعضلة القلب) في البالغين.
- لا يستخدم **فالساتينس** في الأطفال بعمر اقل من ٦ سنوات او الأطفال الذين لديهم بعض المشاكل بالكلى.
- ارتفاع ضغط الدم (ضغط الدم المرتفع).

ضغط الدم هو القوة في الاوعية الدموية عندما يدق قلبك وعندما يستقر قلبك. يكون لديك ارتفاع في ضغط الدم عندما تكون القوة أكثر من اللازم. يمكن ان يساعد فالساتينس اوعيتك الدموية على الارتخاء مما يؤدى الى تقليل ضغط دمك. الادوية التي تقلل من ضغط الدم تقلل من احتمالية الإصابة بالسكتة الدماغية او الازمة القلبية. ارتفاع ضغط الدم يجعل القلب يعمل بشكل كبير لضخ الدم خلال الجسم ويسبب تلف الاوعية الدموية. إذا لم يتم معالجة ضغط الدم المرتفع يمكن ان يؤدى الى سكته دماغية، ازمة قلبية، فشل عضلة القلب، فشل الكلى ومشاكل بالرؤية.

فشل القلب:

يحدث عندما يكون القلب ضعيف ولا يقدر ان يضخ دم كافي الى الرئتين وبقية الجسم. مجرد المشي او الحركة يؤدى الى حدوث ضيق بالنفس، مما يجعلك تحصل على راحة أطول.

الازمة القلبية (جلطة بالقلب):

تحدث الازمة القلبية نتيجة انسداد شريان مما يؤدى الى تلف عضلة القلب.

ما يجب ان أخبره لطبيبي قبل تناول فالساتينس؟

أخبر طبيبك عن حالتك الطبية شاملا إذا كنت:

- لديك أي حساسية. انظر الى اخر النشرة لمعرفة مكونات فالساتينس
- لديك امراض بالقلب.
- لديك مشاكل بالكبد
- لديك مشاكل بالكلى

إذا كنت حاملا أو تخططين لتصبحين حاملا. انظر ما هي اهم المعلومات التي يجب ان اعرفها عن **فالساتينس؟**

- المريضة التي في سن الحمل يطفل يجب ان تخبر عن خطورة التعرض **لفالساتينس** اثناء الحمل.
- يجب ان تناقش اختيارات العلاج مع المريضة التي تخطط للحمل.
- يجب ان تخبر المريضة طبيبها عند حدوث حمل بأسرع ما يمكن.
- إذا كنت تقومين بالرضاعة الطبيعية من غير المعروف إذا كان فالساتينس يفرز في لبن الام.
- يجب ان يقرر وطبيبك إذا كنت سوف تأخذين **فالساتينس** أو تقومين بالرضاعة الطبيعية ولكن ليس كلاهما معا. تكلمي مع طبيبك عن أحسن الطرق لإرضاع طفلك إذا كنت تتناولين **فالساتينس**.
- إذا حدث لك رد فعل يسمى وزمة وعائية لأي من ادوية ضغط الدم.
- الوزمة الوعائية تسبب تورم الوجه، الشفه، اللسان والام الحلق، وتسبب صعوبة في التنفس.
- أخبر طبيبك عن الادوية التي تتناولها شاملا التي بروشته او بدون روشتة الفيتامينات والأدوية العشبية.

اخبر طبيبك بشكل خاص إذا اخذت:

- ادوية أخرى لعلاج ضغط الدم المرتفع او مشاكل بالقلب.
- ادوية لأدرار الماء (تسمى مدرات البول).
- مكملات البوتاسيوم. سوف يقوم طبيبك بفحص كمية البوتاسيوم بالدم لديك بانتظام.
- بديل الملح. سوف يقوم طبيبك بفحص كمية البوتاسيوم بدمك بانتظام.
- مضادات الالتهاب الغير الاستيرودية (مثل ايبيروفين اونابروكسين).
- بعض المضادات الحيوية (مثل مجموعة ريفامبسين). الادوية التي تستخدم للحماية من رفض الزرع (سيكلوسبورين) او عقار مضاد للفيروسات يستخدم لعلاج عدوى فيروس نقص المناعة البشرية الايدز (ريتونفير). هذه الادوية يمكن ان تزيد من تأثير فالسارتان.
- ليثيوم، وهو دواء يستخدم لعلاج الاكتئاب.
- قد يحتاج طبيبك إلى تغيير جرعتك او اتخاذ بعض الاحتياطات:

إذا كنت تتناول مضادات مستقبلات أنجيوتنسين II (ARB) أو مثبطات الانزيم المحول الي الأنجيوتنسين (ACEIs).

- اعرف الادوية التي تتناولها. احتفظ بقائمه لادويتك معك لتريها لطبيبك او الصيدلي عندما يوصف لك دواء جديد.
- تحدث مع طبيبك او الصيدلي قبل تناول أي دواء جديد. سوف يعرف طبيبك او الصيدلي ما هي الادوية الآمنه لتتناولها معا.

كيف يمكن تناول فالساتينس؟

تناول **فالساتينس** تماما كما يصفه طبيبك.

- لعلاج ضغط الدم المرتفع، تناول **فالساتينس** مره واحدة في اليوم، في نفس الميعاد كل يوم.
- إذا كان طفلك لا يستطيع بلع الأقراص او إذا كانت الأقراص غير متوفرة في الجرعة الموصوفة، سوف يقوم الصيدلي بعمل خليط سائل من **فالساتينس** من اجل طفلك.
- إذا كان طفلك انتقل من استعمال المعلق السائل الى الأقراص سوف يقوم طبيبك بضبط الجرعة حسب الاحتياج. رج زجاجة المحلول المعلق جيدا على الأقل لمدة ١٠ ثوان قبل سكب جرعة الدواء لا عطاءها لطفلك.
- للمرضى البالغين الذين يعانون من فشل عضلة القلب او الذين حدث لهم ازمة قلبية، تناول **فالساتينس** مرتين كل يوم. سوف يبدا لك طبيبك الجرعة بجرعة صغيرة من **فالساتينس** وسوف يزيد لك الجرعة اثناء العلاج.
- يمكن تناول **فالساتينس** مع او بدون الطعام.
- إذا نسيت جرعة، تناولها في الحال عند تذكرها. إذا كانت قريبه من ميعاد الجرعة التالية، لا تأخذ الجرعة الفائتة. تناول الجرعة التالية في نفس الميعاد المعتاد.
- إذا تناولت كمية زائدة من **فالساتينس**، اتصل بطبيبك او قسم السموم واذهب الى أقرب مستشفى للطوارئ.
- لا تتناول **فالساتينس** اذا كنت لديك سكر بالدم او نقص في وظائف الكلي او كنت تتعالج بدواء لخفض ضغط الدم التي تحتوي علي اليسكيرين
- المرضى المصابون بأمراض وراثية نادرة مثل عدم تحمل الجالاكتوز، نقص انزيم اللاكتوز، سوء امتصاص جلوكوز - جالاكتوز، يجب عليهم عدم تناول هذا الدواء.

ما هي الاعراض الجانبية المحتملة مع فالساتينس؟

قد يسبب فالساتينس الاعراض الجانبية الاتية:

إصابة او وفاة الطفل قبل الولادة. انظر ماهي المعلومات الهامة التي يجب ان تعرفها عن فالساتينس؟

انخفاض ضغط الدم (ضغط الدم المنخفض).

من المرجح ان يحدث انخفاض ضغط الدم. إذا تناولت حبوبا مدرة لبول او كنت تتناول نظاما غذائيا قليل الملح، قد اجريت غسيل كلى، او تعاني من مشاكل بالقلب او اصبت بالقيء او الاسهال. عليك بالاستلقاء إذا كنت تشعر بالإغماء او الدوار. اتصل بطبيبك في الحال.

مشاكل بالكلى:

مشاكل الكلى يمكن ان تسوء إذا كان لديك امراض بالكلى. بعض المرضى قد يحدث لهم تغييرات في نتائج وظائف الكلى بالدم وقد تحتاج الى جرعات اقل من **فالساتينس**.

اتصل بطبيبك إذا حدث لك تورم في الرجلين، الكاحل، او اليدين او زيادة في الوزن غير مبررة.

إذا كان لديك فشل في عضلة القلب، سوف يقوم طبيبك بفحص كليتك قبل وصف فالساتينس لك.

أكثر الاعراض الجانبية شيوعا للحصول مع فالساتينس لعلاج ضغط الدم المرتفع تشمل:

- الصداع - دوخة - اعراض البرد - تعب - الام المعدة (البطن)
- الام المفاصل والظهر. - ارهاق. - ارتفاع نسبة البوتاسيوم بالدم.
- اسهال.

الاعراض الجانبية الشائعة عند استعمال فالساتينس لعلاج المرضى بعد الازمة القلبية التي تؤدى بهم للتوقف عن تناول الدواء تشمل:

- انخفاض ضغط الدم.
- كحه.
- ارتفاع نسبة الكرياتين بالدم (نقص وظائف الكلى).
- طفح جلدي.

أخبر طبيبك إذا حدثت لك أي من الاعراض الجانبية التي تزعجك او التي لا تختفي.

- هذه ليست كل الاعراض الجانبية الممكنة. بمعرفة بقيتها اسال طبيبك او الصيدلي.

كيف يمكن تخزين فالساتينس

يحفظ في درجة حرارة لا تزيد عن ٢٥ درجه مئويه في مكان جاف

المواد الغير فعالة: فالساتينس ٤٠ مجم: افيسيل PH102، بوفيدون k30، لاكتوز احادي المائيه، كالسيوم هيدروجين فوسفات، كروسكارميللوز الصوديوم، صوديوم ستارش جليكولات، بولوكسامر، تلك منقي ، ستيرات المغنيسيوم، اوبادري ازرق ثاني اوكسيد التيتانيوم.

فالساتينس ٨٠ مجم: افيسيل PH102، بوفيدون، لاكتوز احادي المائيه، كالسيوم هيدروجين فوسفات، كروسكارميللوز الصوديوم، صوديوم ستارش جليكولات، بولوكسامر، تلك منقي ستيرات المغنيسيوم، اوبادري ازرق.

العبوه : علبه كرتون تحتوي علي ٣،٢،١ شرائط (الومنيوم/ بي في سي شفاف / بي في دي سي) كل شريط يحتوي كل منها علي ١٠ اقراص مغلفه + نشره داخليه.

تحفظ جميع الأدوية بعيداً عن متناول الأطفال

إنتاج
شركة آمون للأدوية ش.م.م
مدينة العبور، القليوبية، مصر.

V08-22/6/2023
P150011.00
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Valsatens Film Coated Tablets

Valsartan 40 , 80 mg

Contraindicated in pregnancy as it may cause death or injury to the fetus.

1 INDICATIONS AND USAGE

1.1 Hypertension

Valsatens (valsartan) is indicated for the treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions. These benefits have been seen in controlled trials of antihypertensive drugs from a wide variety of pharmacologic classes including the class to which valsartan principally belongs. There are no controlled trials in hypertensive patients demonstrating risk reduction with **Valsatens**. Control of high blood pressure should be part of comprehensive cardiovascular risk management, including, as appropriate, lipid control, diabetes management, antithrombotic therapy, smoking cessation, exercise, and limited sodium intake. Many patients will require more than one drug to achieve blood pressure goals. For specific advice on goals and management, see published guidelines, such as those of the National High Blood Pressure Education Program's Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC). Numerous antihypertensive drugs, from a variety of pharmacologic classes and with different mechanisms of action, have been shown in randomized controlled trials to reduce cardiovascular morbidity and mortality, and it can be concluded that it is blood pressure reduction, and not some other pharmacologic property of the drugs, that is largely responsible for these benefits. The largest and most consistent cardiovascular outcome benefit has been a reduction in the risk of stroke, but reductions in myocardial infarction and cardiovascular mortality also have been seen regularly. Elevated systolic or diastolic pressure causes increased cardiovascular risk, and the absolute risk increase per mmHg is greater at higher blood pressures, so that even modest reductions of severe hypertension can provide substantial benefit. Relative risk reduction from blood pressure reduction is similar across populations with varying absolute risk, so the absolute benefit is greater in patients who are at higher risk independent of their hypertension (e.g., patients with diabetes or hyperlipidemia), and such patients would be expected to benefit from more aggressive treatment to a lower blood pressure goal. Some antihypertensive drugs have smaller blood pressure effects (as monotherapy) in black patients, and many antihypertensive drugs have additional approved indications and effects (e.g., on angina, heart failure, or diabetic kidney disease). These considerations may guide selection of therapy.

Valsatens may be used alone or in combination with other antihypertensive agents.

1.2 Heart Failure

Valsatens is indicated for the treatment of heart failure (NYHA class II-IV). In a controlled clinical trial, **Valsatens** significantly reduced hospitalizations for heart failure. There is no evidence that **Valsatens** provides added benefits when it is used with an adequate dose of an ACE inhibitor (see Clinical Studies 14.2).

1.3 Post-Myocardial Infarction

In clinically stable patients with left ventricular failure or left ventricular dysfunction following myocardial infarction, **Valsatens** is indicated to reduce cardiovascular mortality (see Clinical Studies 14.3).

2 DOSAGE AND ADMINISTRATION

2.1 Adult Hypertension

The recommended starting dose of **Valsatens** is 80 mg or 160 mg once daily when used as monotherapy in patients who are not volume-depleted. Patients requiring greater reductions may be started at the higher dose. Valsartan may be used over a dose range of 80 mg to 320 mg daily, administered once a day. The antihypertensive effect is substantially present within 2 weeks and maximal reduction is generally attained after 4 weeks. If additional antihypertensive effect is required over the starting dose range, the dose may be increased to a maximum of 320 mg or a diuretic may be added. Addition of a diuretic has a greater effect than dose increases beyond 80 mg. No initial dosage adjustment is required for elderly patients, for patients with mild or moderate renal impairment, or for patients with mild or moderate liver insufficiency. Care should be exercised with dosing of **Valsatens** in patients with hepatic or severe renal impairment.

Valsatens may be administered with other antihypertensive agents.

Valsatens may be administered with or without food.

2.2 Pediatric Hypertension 6 to 16 Years of Age

For children who can swallow tablets, the usual recommended starting dose is 1.3 mg/kg once daily (up to 40 mg total). The dosage should be adjusted according to blood pressure response. Doses higher than 2.7 mg/kg (up to 160 mg) once daily have not been studied in pediatric patients 6 to 16 years old. For children who cannot swallow tablets, or children for whom the calculated dosage (mg/kg) does not correspond to the available tablet strengths of Valsartan, the use of a suspension is recommended. Follow the suspension preparation instructions below (see **Preparation of Suspension**) to administer valsartan as a suspension. When the suspension is replaced by a tablet, the dose of valsartan may have to be increased. The exposure to valsartan with the suspension is 16 times greater than with the tablet. No data are available in pediatric patients either undergoing dialysis or with a glomerular filtration rate <30 mL/min/1.73 m^2 (see *Pediatric Use 8.4*).

Valsatens is not recommended for patients <6 years old (see *Adverse Reactions 6.1*), Clinical Studies *14.11*).

Preparation of Suspension (for 160 ml, of a 8 mg/ml, suspension)

Add 80 ml, of Ora-Plus ® oral suspending vehicle to an amber glass bottle containing 8 **Valsatens** 80 mg tablets, and shake for a minimum of 2 minutes. Allow the suspension to stand for a minimum of 1 hour. After the standing time, shake the suspension for a minimum of 1 additional minute. Add 80 ml, of Ora-Sweet SF® oral-sweetening vehicle to the bottle and shake the suspension for at least 30 seconds to disperse the ingredients. The suspension is homogeneous and can be stored for either up to 30 days at room temperature (below 30°C/86°F) or up to 75 days at refrigerated conditions (2°C/35-46°F) in the original bottle with child-resistant screw-cap closure. Shake the bottle well (at least 10 seconds) prior to dispensing the suspension.

2.3 Heart Failure

The recommended starting dose of Valsartan is 40 mg twice daily. Uptitration to 80 mg and 160 mg twice daily should be done to the highest dose, as tolerated by the patient. Consideration should be given to reducing the dose of concomitant diuretics. The maximum daily dose administered in clinical trials is 320 mg in divided doses.

2.4 Post-Myocardial Infarction

Valsatens may be initiated as early as 12 hours after a myocardial infarction. The recommended starting dose of Valsartan is 20 mg twice daily. Patients may be uptitrated within 7 days to 40 mg twice daily, with subsequent titrations to a target maintenance dose of 160 mg twice daily, as tolerated by the patient. If symptomatic hypotension or renal dysfunction occurs, consideration should be given to a dosage reduction. Valsatens may be given with other standard post-myocardial infarction treatment, including thrombolytics, aspirin, beta-blockers, and statins.

3 CONTRAINDICATIONS

You have diabetes or impaired kidney function & You are treated with a blood pressure lowering medicine containing aliskiren.

Do not use in patients with known hypersensitivity to any component.

Do not coadminister aliskiren with **Valsatens** in patients with diabetes (see *Drug Interactions 7*).

The concomitant use of Valsartan with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60ml/min/1.73m2).

4 WARNINGS AND PRECAUTIONS

4.1 Fetal Toxicity

Pregnancy Category D

Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue **Valsatens** as soon as possible (see *Use in Specific Populations 8.1*).

4.2 Hypotension

Excessive hypotension was rarely seen (0.1%) in patients with uncomplicated hypertension treated with Valsartan alone. In patients with an activated renin-angiotensin system, such as volume-and/or salt-depleted patients receiving high doses of diuretics, symptomatic hypotension may occur. This condition should be corrected prior to administration of **Valsatens**, or the treatment should start under close medical supervision.

Caution should be observed when initiating therapy in patients with heart failure or post-myocardial infarction patients. Patients with heart failure or post-myocardial infarction patients given **Valsatens** commonly have some reduction in blood pressure, but discontinuation of therapy because of continuing symptomatic hypotension usually is not necessary when dosing instructions are followed. In controlled trials in heart failure patients, the incidence of hypotension in valsartan-treated patients was 5.5% compared to 1.8% in placebo-treated patients. In the Valsartan in Acute Myocardial Infarction Trial (VALIANT), hypotension in post-myocardial infarction patients led to permanent discontinuation of therapy in 1.8% of valsartan-treated patients and 0.8% of captopril-treated patients. If excessive hypotension occurs, the patient should be placed in the supine position and, if necessary, given an intravenous infusion of normal saline. A transient hypotonic response is not a contraindication to further treatment, which usually can be continued without difficulty once the blood pressure has stabilized.

4.3 Impaired Renal Function

Changes in renal function including acute renal failure can be caused by drugs that inhibit the renin-angiotensin system and by diuretics. Patients whose renal function may depend in part on the activity of the renin-angiotensin system (e.g., patients with renal artery stenosis, chronic kidney disease, severe congestive heart failure, or volume depletion) may be at particular risk of developing acute renal failure on **Valsatens**. Monitor renal function periodically in these patients. Consider withholding or discontinuing therapy in patients who develop a clinically significant decrease in renal function on **Valsatens** (see *Drug Interactions 7*).

4.4 Hyperkalemia

Some patients with heart failure have developed increases in potassium. These effects are usually minor and transient, and they are more likely to occur in patients with pre-existing renal impairment. Dosage reduction and/or discontinuation of **Valsatens** may be required (see *Adverse Reactions 6.1*).

4.5 Dual blockade of the renin-angiotensin-aldosterone system (RAAS)

There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is therefore not recommended. If dual blockade therapy is considered absolutely necessary, this should only occur under specialist supervision and subject to frequent close monitoring of renal function, electrolytes and blood pressure. ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.

4.6 Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

5 ADVERSE REACTIONS

5.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug, and may not reflect the rates observed in practice.

Adult Hypertension

Valsartan has been evaluated for safety in more than 4,000 patients, including over 400 treated for over 6 months, and more than 360 for over 1 year. Adverse reactions have generally been mild and transient in nature and have only infrequently required discontinuation of therapy. The overall incidence of adverse reactions with Valsartan was similar to placebo. The overall frequency of adverse reactions was neither dose-related nor related to gender, age, race, or regimen. Discontinuation of therapy due to side effects was required in 2.3% of valsartan patients and 2.0% of placebo patients. The most common reasons for discontinuation of therapy with Valsartan were headache and dizziness. The adverse reactions that occurred in patients treated with Valsartan included viral infection, fatigue, and abdominal pain. Headache, dizziness, upper respiratory infection, cough, diarrhea, rhinitis, sinusitis, nausea, pharyngitis, edema, and arthralgia occurred at a more than 1% rate but at about the same incidence in placebo and valsartan patients. In trials in which valsartan was compared to an ACE inhibitor with or without placebo, the incidence of dry cough was significantly greater in the ACE inhibitor group (7.9%) than in the groups who received valsartan (2.6%) or placebo (1.5%). In a 329-patient trial limited to patients who had had dry cough when they had previously received ACE inhibitors, the incidences of cough in patients who received valsartan, HCTZ, or lisinopril were 20%, 19%, and 69% respectively. (p <0.001). Dose-related orthostatic effects were seen in less than 1% of patients. An increase in the incidence of dizziness was observed in patients treated with Valsartan 320 mg (4%) compared to 1% for 160 mg (2%) or 80 mg.

Valsatens has been used concomitantly with hydrochlorothiazide without evidence of clinically important adverse interactions.

Body as a Whole: Allergic reaction and asthenia **Cardiovascular:** Palpitations **Dermatologic:** Pruritus and rash **Digestive:** Constipation, dry mouth, dyspepsia, and flatulence **Musculoskeletal:** Back pain, muscle cramps, and myalgia **Neurologic and Psychiatric:** Anxiety, insomnia, paresthesia, and somnolence **Respiratory:** Dyspnea **Special Senses:** Vertigo **Urogenital:** Impotence.

Other reported events seen less frequently in clinical trials included chest pain, syncope, anorexia, vomiting, and angioedema.

Pediatric Hypertension: Valsartan has been evaluated for safety in over 400 pediatric patients aged 6 to 17 years and more than 360 pediatric patients aged 6 months to 5 years. No relevant differences were identified between the adverse experience profile for pediatric patients aged 6 to 16 years and that previously reported for adult patients. Headache and hyperkalaemia were the most common adverse events suspected to be study drug-related in older children (6 to 17 years old) and younger children (6 months to 5 years old), respectively. Hyperkalaemia was mainly observed in children with underlying renal disease. Neurocognitive and developmental assessment of pediatric patients aged 6 to 16 years revealed no overall clinically relevant adverse impact after treatment with Valsartan for up to 1 year. Valsartan is not recommended for pediatric patients under 6 years of age. In a study (n=90) of pediatric patients (1 to 5 years), two deaths and three cases of un-treatment transaminase elevations were seen in the one-year open-label extension phase. These 5 events occurred in a study population in which patients frequently had significant co-morbidities. A causal relationship to Valsartan has not been established. In a second study of 6-months duration in 75 children aged 1 to 5 years, there were no deaths; one case of marked liver transaminase elevations occurred following 6 months of treatment.

Heart Failure: The adverse experience profile of Valsartan in heart failure patients was consistent with the pharmacology of the drug and the health status of the patients. In the Valsartan Heart Failure Trial, comparing valsartan in total daily doses up to 320 mg (n=2,506) to placebo (n=2,494), 30% of valsartan patients discontinued for adverse reactions vs. 7% of placebo patients.

The table shows adverse reactions including the first 6 months of the Valsartan Heart Failure Trial. All patients received standard drug therapy for heart failure, frequently on multiple medications, which could include diuretics, digitalis, beta blockers, about 93% of patients received concomitant ACE inhibitors.

Valsartan
Dizziness
Hypotension
Asthenia
Arthrosis
Fatigue
Back pain
Diarrhea, postural
Hypotension
Hypotension, postural

Discontinuations occurred in 0.7% of valsartan-treated patients and 0.1% of placebo patients for each of the following: elevations in creatinine and elevations in potassium.

Other adverse reactions with an incidence greater than 1% and greater than placebo included headache (6.0%), nausea, renal impairment (4.0%), syncope, blurred vision, upper abdominal pain and vertigo (NOS = not otherwise specified). From the long-term data in the Valsartan Heart Failure Trial, there did not appear to be any significant adverse reactions not previously identified.

Post-Myocardial Infarction

The safety profile of Valsartan was consistent with the pharmacology of the drug and the background diseases, cardiovascular risk factors, and clinical course of patients treated in the post-myocardial infarction setting. The table shows the percentage of patients discontinued in the valsartan and captopril-treated groups in the Valsartan in Acute Myocardial Infarction Trial (VALIANT) with a rate of at least 0.5% in either of the treatment groups.

Discontinuations due to renal dysfunction occurred in 1.1% of valsartan-treated patients and 0.8% of captopril-treated patients.

	Valsartan (n=4,885)	Captopril (n=4,879)
Discontinuation for adverse reaction	5.0%	9.2%
Adverse reactions		
Hypotension NOS	1.4%	0.8%
Cough	0.6%	2.2%
Blood creatinine increased	0.0%	0.4%
RDR NOS	0.2%	0.6%

5.2 Postmarketing Experience

The following additional adverse reactions have been reported in postmarketing experience:

Hypersensitivity: There are rare reports of angioedema. Some of these patients previously experienced angioedema with other drugs including ACE inhibitors. Dyspnea should not be re-administered to patients who have had angioedema. **Digestive:** Elevated liver enzymes and very rare reports of hepatitis **Renal:** Impaired renal function, renal failure **Clinical Laboratory Tests:** Hyperkalemia **Dermatologic:** Alopecia, bullous dermatitis **Blood and Lymphatic:** There are very rare reports of thrombocytopenia **Vascular:** Vasculitis

Rare cases of rhabdomyolysis have been reported in patients receiving angiotensin II receptor blockers. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

6 DRUG INTERACTIONS

No clinically significant pharmacokinetic interactions were observed when valsartan was coadministered with amlodipine, atenolol, cimetidine, digoxin, furosemide, glyburide, hydrochlorothiazide, or indomethacin. The valsartan/amlodipine combination was more antihypertensive than either component, but it did not lower the heart rate more than atenolol alone. Coadministration of valsartan and warfarin did not change the pharmacokinetics of valsartan or the time-course of the anticoagulant properties of warfarin. CYP 450 Interactions: In vitro metabolism studies indicate that CYP 450 mediated drug interactions between valsartan and coadministered drugs are unlikely because of the low extent of metabolism (see Clinical Pharmacology 12.3).

Transporters: The results from an in vitro study with human liver tissue indicate that valsartan is a substrate of the hepatic uptake transporter OATP1B1 and the hepatic efflux transporter MRP2. Coadministration of inhibitors of the uptake transporter rifampin, cyclosporine or efflux transporter irbesartan may increase the systemic exposure to valsartan.

Potassium: Concomitant use of valsartan with other agents that block the renin-angiotensin system, potassium-sparing diuretics (e.g., spironolactone, triamterene, amiloride), potassium supplements, salt substitutes containing potassium or other drugs that may increase potassium levels (e.g., heparin) may lead to increases in serum potassium and in heart failure patients to increases in serum creatinine. If co-medication is considered necessary, monitoring of serum potassium is advisable.

Non-Steroidal Anti-Inflammatory Agents including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors): In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, coadministration of NSAIDs, including selective COX-2 inhibitors, with angiotensin II receptor antagonists, including valsartan, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically in patients receiving valsartan and NSAID therapy.

The antihypertensive effect of angiotensin II receptor antagonists, including valsartan, may be attenuated by NSAIDs including selective COX-2 inhibitors.

Dual Blockade of the Renin-Angiotensin System (RAS): Dual blockade of the RAS with angiotensin receptor blockers, ACE inhibitors, or aliskiren is associated with increased risks of hypotension, hyperkalemia, and changes in renal function (including acute renal failure) compared to monotherapy. Most patients receiving the combination of two RAS inhibitors do not obtain any additional benefit compared to monotherapy (see *Clinical Trials 14.3*). In general, avoid combined use of RAS inhibitors. Closely monitor blood pressure, renal function and electrolytes in patients on Valsartan and other agents that affect the RAS.

Do not coadminister aliskiren with Valsartan in patients with diabetes. Avoid use of aliskiren with Valsartan in patients with renal impairment (GFR <60 mL/min).

Lithium: Increases in serum lithium concentrations and lithium toxicity have been reported during concomitant administration of lithium with angiotensin II receptor antagonists, including Valsartan. Monitor serum lithium levels during concomitant use.

6.1 Clinical Laboratory Test Findings

In controlled clinical trials, clinically important changes in standard laboratory parameters were rarely associated with administration of Valsartan.

Creatinine: Minor elevations in creatinine occurred in 0.05% of patients taking Valsartan and 0.6% given placebo in controlled clinical trials of hypertensive patients. In heart failure trials, greater than 50% increases in serum creatinine were observed in 1.2% of Valsartan-treated patients compared to 0.9% of placebo-treated patients. In post-myocardial infarction patients, doubling of serum creatinine was observed in 4.2% of valsartan-treated patients and 5.4% of captopril-treated patients.

Hemoglobin and Hematocrit: Greater than 20% decreases in hemoglobin and hematocrit were observed in 0.4% and 0.8%, respectively, of Valsartan patients, compared with 0.1% and 0.1% in placebo-treated patients. One valsartan patient discontinued treatment for microcytic anemia.

Liver Function Tests: Occasional elevations (greater than 150%) of liver chemistries occurred in Valsartan -treated patients. Three patients (<0.1%) treated with valsartan discontinued treatment for elevated liver chemistries.

Neutropenia: Neutropenia was observed in 1.9% of patients treated with Valsartan and 0.8% of patients treated with placebo.

Serum Potassium: In hypertensive patients, greater than 20% increases in serum potassium were observed in 4.4% of Valsartan -treated patients compared to 2.9% of placebo-treated patients. In heart failure patients, greater than 20% increases in serum potassium were observed in 10.0% of Valsartan -treated patients compared to 5.1% of placebo-treated patients.

Blood Urea Nitrogen (BUN): In heart failure trials, greater than 50% increases in BUN were observed in 16.6% of Valsartan -treated patients compared to 6.5% of placebo-treated patients.

7 USE IN SPECIFIC POPULATIONS

7.1 Pregnancy

Pregnancy Category D

Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue **Valsatens** as soon as possible. These adverse outcomes are usually associated with use of these drugs in the second and third trimesters of pregnancy. Most epidemiologic studies examining fetal abnormalities after exposure to antihypertensive use in the first trimester have not distinguished drugs affecting the renin-angiotensin system from other antihypertensive agents. Appropriate management of maternal hypertension during pregnancy is important to optimize outcomes for both mother and fetus. In the unusual case that there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system for a particular patient, apprise the mother of the potential risk to the fetus. Perform serial ultrasound examinations to assess the intra-amniotic environment. If oligohydramnios is observed, discontinue Valsartan, unless it is considered lifesaving for the mother. Fetal testing may be appropriate, based on the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury. Closely observe infants with histories of in utero exposure to Valsartan for hypotension, oliguria, and hyperkalemia (see *Use in Specific Populations 8.6*). **Nursing Mothers:** It is not known whether **Valsatens** is excreted in human milk. Because many drugs are excreted into human milk and because of the potential for adverse reactions in nursing infants from **Valsatens**, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

7.2 Pediatric Use

Valsartan was generally well tolerated in children 6–16 years and the adverse experience profile was similar to that described for adults.

In children and adolescents with hypertension where underlying renal abnormalities may be more common, renal function and serum potassium should be closely monitored as clinically indicated. **Valsatens** is not recommended for pediatric patients under 6 years of age due to safety findings for which a relationship to treatment could not be excluded (see *Adverse Reactions, Pediatric Hypertension 6.1*). No data are available in pediatric patients either undergoing dialysis or with a glomerular filtration rate <30 mL/min/1.73 m_2. There is limited clinical experience with Valsartan in pediatric patients with mild to moderate hepatic impairment (see *Warnings and Precautions 5.5*).

Neonates with a history of in utero exposure to Valsartan:

If oliguria or hypotension occurs, direct attention toward support of blood pressure and renal perfusion. Exchange transfusions or dialysis may be required as a means of reversing hypotension and/or substituting for disordered renal function.

7.3 Geriatric Use

In the controlled clinical trials of valsartan, 1,214 (36.2%) hypertensive patients treated with valsartan were ≥65 years and 265 (7.9%) were ≥75 years. No overall difference in the efficacy or safety of valsartan was observed in this patient population, but greater sensitivity of some older individuals cannot be ruled out. Of the 2,511 patients with heart failure randomized to valsartan in the Valsartan Heart Failure Trial, 45% (1,141) were 65 years of age or older. In the Valsartan in Acute Myocardial Infarction Trial (VALIANT), 33% (2,596) of the 4,909 patients treated with valsartan and 35% (2,353) of the 4,885 patients treated with valsartan + captopril were 65 years of age or older. There were no notable differences in efficacy or safety between older and younger patients in either trial.

7.4 Renal Impairment

Safety and effectiveness of Valsartan in patients with severe renal impairment (CrCl 30 mL/min) have not been established. No dose adjustment is required in patients with mild (CrCl 60 to 90 mL/min) or moderate (CrCl 30 to 60 mL/min) renal impairment.

7.5 Hepatic Impairment

No dose adjustment is necessary for patients with mild-to-moderate liver disease. No dosing recommendations can be provided for patients with severe liver disease.

8 OVERDOSAGE

Limited data are available related to overdosage in humans. The most likely manifestations of overdosage would be hypotension and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. Depressed level of consciousness, circulatory collapse and shock have been reported. If symptomatic hypotension should occur, supportive treatment should be instituted. Dosage (valsartan) is not removed from the plasma by hemodialysis. Valsartan was without grossly observable adverse effects at single oral doses up to 2000 mg/kg in rats and up to 1000 mg/kg in marmosets, except for salivation and diarrhea in the cat and vomiting in the marmoset at the highest dose (60 and 31 times, respectively, the maximum recommended human dose on a mg/m2 basis). (Calculations assume an oral dose of 320 mg/day and a 60 kg patient).

9 CLINICAL PHARMACOLOGY

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