A clinically meaningful reduction of 50 % of biochemical markers of bone resorption was observed as early as one month after starting treatment with ibandronic acid 2.5 mg.

Paediatric population (see section 4.2 and section 5.2).
Bondenza was not studied in the paediatric population, therefore no efficacy or safety data are available for this patient population

5.2 Pharmacokinetic properties

The primary pharmacological effects of ibandronic acid on bone are not directly related to actual plasma concentrations, as demonstrated by various studies in animals and humans.

Plasma concentrations of ibandronic acid increase in a dose-proportional manner after intravenous administration of 0.5 mg to 6 mg.

Absorption
Not applicable

Distribution
After initial systemic exposure, ibandronic acid rapidly binds to bone or is excreted into urine. In humans, the apparent terminal volume of distribution is at least 90 l and the amount of dose reaching the bone is estimated to be 40 – 50 % of the circulating dose. Protein binding in human plasma is approximately 85 % - 87 % (determined *in vitro* at therapeutic ibandronic acid concentrations), and thus there is a low potential for interaction with other medicinal products due to displacement.

Biotransformation
There is no evidence that ibandronic acid is metabolised in animals or humans.

Elimination
Ibandronic acid is removed from the circulation via bone absorption (estimated to be 40 – 50 % in postmenopausal women) and the remainder is eliminated unchanged by the kidney.

The range of observed apparent half-lives is broad, the apparent terminal half-life is generally in the range of 10 - 72 hours. As the values calculated are largely a function of the duration of study, the dose used, and assay sensitivity, the true terminal half-life is likely to be substantially longer, in common with other bisphosphonates. Early plasma levels fall quickly, reaching 10 % of the peak values within 3 and 8 hours after intravenous or oral administration, respectively.

Total clearance of ibandronic acid is low with average values in the range 84 - 160 ml/min. Renal clearance (about 60 ml/min in healthy postmenopausal females) accounts for 50 – 60 % of total clearance, and is related to creatinine clearance. The difference between the apparent total and renal clearances is considered to reflect the uptake by bone.

The secretory pathway appears not to include known acidic or basic transport systems involved in the excretion of other active substances.(see section 4.5). In addition, ibandronic acid does not inhibit the major human hepatic P450 isoenzymes and does not induce the hepatic cytochrome P450 system in rats.

<u>Pharmacokinetics in special clinical situations</u>

Gender
Pharmacokinetics of ibandronic acid are similar in men and women.

Race
There is no evidence for any clinically relevant inter-ethnic differences between Asians and Caucasians in ibandronic acid disposition. There is limited data available on patients of African origin.

Patients with renal impairment
Renal clearance of ibandronic acid in patients with various degrees of renal impairment is linearly related to creatinine clearance (CLcr).

No dose adjustment is necessary for patients with mild or moderate renal impairment (CLcr equal or above 30 ml/min).

Subjects with severe renal impairment (CLcr less than 30 ml/min) receiving daily oral administration of 10 mg ibandronic acid for 21 days, had 2 - 3 fold higher plasma concentrations than subjects with normal renal function and total clearance of ibandronic acid was 44 ml/min. After intravenous administration of 0.5 mg of ibandronic acid, total, renal, and non-renal clearances decreased by 67 %, 77 % and 50 %, respectively, in subjects with severe renal failure, but there was no reduction in tolerability associated with the increase in exposure. Due to the limited clinical experience, Bondenza is not recommended in patients with severe renal impairment (see section 4.2 and section 4.4). The pharmacokinetics of ibandronic acid in patients with end-stage renal disease was only assessed in a small number of patients managed by haemodialysis, therefore, the pharmacokinetics of ibandronic acid in the patients not undergoing haemodialysis is unknown. Due to the limited data available, ibandronic acid should not be used in all patients with end-stage renal disease.

Patients with hepatic impairment (see section 4.2)

There are no pharmacokinetic data for ibandronic acid in patients who have hepatic impairment. The liver has no significant role in the clearance of ibandronic acid, which is not metabolised but is cleared by renal excretion and by uptake into bone. Therefore dose adjustment is not necessary in patients with hepatic impairment.

Elderly population (see section 4.2)
In a multivariate analysis, age was not found to be an independent factor of any of the pharmacokinetic parameters studied. As renal function decreases with age, renal function is the only factor to take into consideration (see renal impairment section).

Paediatric population (see section 4.2 and section 5.1)
There are no data on the use of Bondenza in these age groups.

5.3 Preclinical safety data

Toxic effects, e.g. signs of renal damage, were observed in dogs only at exposures considered sufficiently in excess of the maximum human exposure, indicating little relevance to clinical use.

Mutagenicity/Carcinogenicity:
No indication of carcinogenic potential was observed. Tests for genotoxicity revealed no evidence of genetic activity for ibandronic acid.

Reproductive toxicity:
Specific studies for the 3-monthly dosing regimen have not been performed. In studies with daily i.v. dosing regimen, there was no evidence for a direct foetal toxic or teratogenic effect of ibandronic acid in rats and rabbits. Body weight gain was decreased in F_1 offspring in rats. In reproductive studies in rats by the oral route effects on fertility consisted of increased preimplantation losses at dose levels of 1 mg/kg/day and higher. In reproductive studies in rats by the intravenous route, ibandronic acid decreased sperm counts at doses of 0.3 and 1 mg/kg/day and decreased fertility in males at 1 mg/kg/day and in females at 1.2 mg/kg/day. Other adverse reactions to ibandronic acid in reproductive toxicity studies in the rat were those observed with bisphosphonates as a class. They include a decreased number of implantation sites, interference with natural delivery (dystocia), and an increase in visceral variations (renal pelvis ureter syndrome).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Glacial acetic acid
Sodium acetate trihydrate
Water for injections

6.2 Incompatibilities

Bondenza solution for injection must not be mixed with calcium-containing solutions or other intravenously administered medicinal products.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Pre-filled syringes (5 ml) made of colourless type I glass, the grey rubber plunger stopper and tip cap are made of fluororesin-laminated butyl rubber, containing 3 ml of solution for injection.
Packs of 1 pre-filled syringe and 1 injection needle or 4 pre-filled syringes and 4 injection needles.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Where the medicinal product is administered into an existing intravenous infusion line, the infusate should be restricted to either isotonic saline or 50 mg/ml (5 %) glucose solution. This also applies to solutions used to flush butterfly and other devices.

Any unused solution for injection, syringe and injection needle should be disposed of in accordance with local requirements. The release of pharmaceuticals in the environment should be minimized.

The following points should be strictly adhered to regarding the use and disposal of syringes and other medicinal sharps:

- Needles and syringes should never be reused.
- Place all used needles and syringes into a sharps container (puncture-proof disposable container).
- Keep this container out of the reach of children.
- Placing used sharps containers in the household waste should be avoided.
- Dispose of the full container according to local requirements or as instructed by your healthcare provider.

7. MARKETING AUTHORISATION HOLDER

Roche Registration Limited
6 Falcon Way
Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/03/266/005
EU/1/03/266/006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23.02.2004
Date of latest renewal: 20.02.2009

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Film-coated tablet:

Roche Pharma AG
Emil-Barell-Strasse 1
D-79639 Grenzach-Wyhlen
Germany

Solution for injection in pre-filled syringe:

Roche Pharma AG
Emil-Barell-Strasse 1
D-79639 Grenzach-Wyhlen
Germany

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

Pharmacovigilance system
The MAH must ensure that the system of pharmacovigilance, presented in Module 1.8.1. of the Marketing Authorisation, is in place and functioning before and whilst the medicinal product is on the market.

Risk Management Plan (RMP)
The MAH shall perform the pharmacovigilance activities detailed in the Pharmacovigilance Plan, as agreed in the RMP presented in Module 1.8.2 of the Marketing Authorisation and any subsequent updates of the RMP agreed by the Committee for Medicinal Products for Human Use (CHMP).

As per the CHMP Guideline on Risk Management Systems for medicinal products for human use, the updated RMP should be submitted at the same time as the next Periodic Safety Update Report (PSUR).

In addition, an updated RMP should be submitted:

- When new information is received that may impact on the current Safety Specification, Pharmacovigilance Plan or risk minimisation activities
- Within 60 days of an important (pharmacovigilance or risk minimisation) milestone being reached
- At the request of the European Medicines Agency.

PSURs
The marketing authorisation holder shall submit PSURs for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Bondenza 150 mg film-coated tablets
Ibandronic acid

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 150 mg ibandronic acid (as sodium monohydrate).

3. LIST OF EXCIPIENTS

The tablets also contain lactose. See the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Film-coated tablets
1 film-coated tablet
3 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Do not suck, chew or crush tablets
Read the package leaflet before use
Once monthly tablet
Oral use

Month 1 __/__/__ 3 film-coated tablets
Month 2 __/__/__ 3 film-coated tablets
Month 3 __/__/__ 3 film-coated tablets
Note down the date you take your tablet

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Roche Registration Limited
6 Falcon Way
Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/03/266/003 1 film-coated tablet
EU/1/03/266/004 3 film-coated tablets

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Bondenza 150 mg

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

Blister foil

1. NAME OF THE MEDICINAL PRODUCT

Bondenza 150 mg film-coated tablets
Ibandronic acid

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Roche Registration Ltd.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

Bondenza 3 mg solution for injection
Ibandronic acid

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe of 3 ml solution contains 3 mg of ibandronic acid (as sodium monohydrate).

3. LIST OF EXCIPIENTS

Also contains sodium chloride, glacial acetic acid, sodium acetate trihydrate, water for injections. See the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
1 pre-filled syringe + 1 injection needle
4 pre-filled syringes + 4 injection needles

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use
For intravenous use only

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Roche Registration Limited
6 Falcon Way
Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/03/266/005 1 pre-filled syringe
EU/1/03/266/006 4 pre-filled syringes

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[Justification for not including Braille accepted]

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Bondenza 3 mg solution for injection
Ibandronic acid
For IV use only

2. METHOD OF ADMINISTRATION

Read the package leaflet before use

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

3 mg/3 ml

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Bondenza
150 mg film-coated tablets
Ibandronic acid

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet:
Planning when to take Bondenza
with peel-off stickers for your personal calendar

1. What Bondenza is and what it is used for

Bondenza belongs to a group of medicines called bisphosphonates. It contains the active substance ibandronic acid. Bondenza may reverse bone loss by stopping more loss of bone and increasing bone mass in most women who take it, even though they won't be able to see or feel a difference. Bondenza may help lower the chances of breaking bones (fractures). This reduction in fractures was shown for the spine but not for the hip.

Bondenza is prescribed to you to treat postmenopausal osteoporosis because you have an increased risk of fractures. Osteoporosis is a thinning and weakening of the bones, which is common in women after the menopause. At the menopause, a woman's ovaries stop producing the female hormone, oestrogen, which helps to keep her skeleton healthy.

The earlier a woman reaches the menopause, the greater her risk of fractures in osteoporosis.

Other things that can increase the risk of fractures include:
- not enough calcium and vitamin D in the diet
- smoking, or drinking too much alcohol
- not enough walking or other weight-bearing exercise
- a family history of osteoporosis

.**A healthy lifestyle** will also help you to get the most benefit from your treatment. This includes:
- eating a balanced diet rich in calcium and vitamin D
- walking or any other weight-bearing exercise
- not smoking; and not drinking too much alcohol

2. What you need to know before you take Bondenza

Do not take Bondenza
- If you are allergic to ibandronic acid, or any of the other ingredients of this medicine listed in section 6).
- If you have certain problems with your gullet/food pipe (oesophagus) such as narrowing or difficulty swallowing.
- If you can't stand or sit upright for at least one hour (60 minutes) at a time.
- **If you have, or had in the past low blood calcium**. Please consult your doctor.

Warnings and precautions
Some people need to be especially careful while they're taking Bondenza. Talk to your doctor before taking Bondenza:
- If you have any disturbances of mineral metabolism (such as vitamin D deficiency).
- If your kidneys are not functioning normally.
- If you have any swallowing or digestive problems.
- If you are under dental treatment or will undergo dental surgery, tell your dentist that you are being treated with Bondenza.

Irritation, inflammation or ulceration of the gullet/food pipe (oesophagus) often with symptoms of severe pain in the chest, severe pain after swallowing food and/or drink, severe nausea, or vomiting may occur, especially if you do not drink a full glass of water and/or if you lie down within an hour of taking Bondenza. If you develop these symptoms, stop taking Bondenza and tell your doctor straight away (see section 3).

Children and adolescents
Do not give Bondenza to children or adolescents below 18 years.

Other medicines and Bondenza
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Especially:

- **Supplements containing calcium, magnesium, iron or aluminium**, as they could possibly influence the effects of Bondenza.

- Acetylsalicylic acid and other non-steroidal anti-inflammatory medicines (NSAIDs) (including ibuprofen, diclofenac sodium and naproxen) may irritate the stomach and intestine. Bisphosphonates (like Bondenza) may also do so. So be especially careful if you take painkillers or anti-inflammatories while you're taking Bondenza.

After swallowing your monthly Bondenza tablet, **wait for 1 hour before taking any other medication**, including indigestion tablets, calcium supplements, or vitamins.

Bondenza with food and drink:
Do not take Bondenza with food. Bondenza is less effective if it's taken with food.
You can drink water but no other drinks (see 3. How to take Bondenza).

Pregnancy and breast feeding
Do not take Bondenza if you're pregnant or breast feeding. If you're breast feeding, you may need to stop in order to take Bondenza.
Ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
You can drive and use machines as it's expected that Bondenza has no or negligible effect on your ability to drive and use machines.

Bondenza contains lactose.
If you have been told by your doctor that you cannot tolerate or digest some sugars (e.g. if you have a galactose intolerance, the Lapp lactase deficiency or have problems with glucose-galactose absorption), talk to your doctor before taking this medicine.

3. How to take Bondenza

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The usual dose of Bondenza is one tablet once a month.

Taking your monthly tablet
It's important to follow these instructions carefully. They are designed to help your Bondenza tablet reach your stomach quickly, so it's less likely to cause irritation.

- **Take one Bondenza 150 mg tablet once a month.**
- **Choose one day of the month** that will be easy to remember. You can choose either the same date (such as the 1st of each month) or the same day (such as the first Sunday of each month) to take your Bondenza tablet. Choose the date that best fits your routine.
- Take your Bondenza tablet **at least 6 hours after you last had anything** to eat or drink except water.

- Take your Bondenza tablet
  - **after you first get up for the day**, and
  - **before you have anything to eat or drink** (on an empty stomach)

- **Swallow your tablet with a full glass of water** (at least 180 ml).

Do not take your tablet with l water with a high concentration of calcium, fruit juice or any other drinks. If there is a concern regarding potentially high levels of calcium in the tap water (hard water), it is advised to use bottled water with a low mineral content.

- **Swallow your tablet whole** — do not chew it, crush it or let it dissolve in your mouth.

- **For the next hour (60 minutes)** after you've taken your tablet
  - **do not lie down**; if you do not stay upright (standing or sitting), some of the medicine could leak back into your oesophagus

  - **do not eat anything**

  - **do not drink anything** (except water if you need it)
  - **do not take any other medicines**

- After you've waited for an hour, you can have your first food and drink of the day. Once you've eaten, it's OK to lie down if you wish, and to take any other medication you need.

Do not take your tablet at bedtime or before you get up for the day.

Continuing to take Bondenza
It's important to keep taking Bondenza every month, as long as your doctor prescribes it for you. Bondenza can treat osteoporosis only as long as you keep taking it.

If you take more Bondenza than you should
If you've taken more than one tablet by mistake, **drink a full glass of milk and talk to your doctor straight away.**

Do not make yourself vomit, and do not lie down — this could cause Bondenza to irritate your oesophagus.

If you forget to take Bondenza
If you forget to take your tablet on the morning of your chosen day, **do not take a tablet later in the day**. Instead, consult your calendar and find out when your next scheduled dose is.

If your next scheduled dose is only 1 to 7 days away…
You should wait until the next scheduled dose is due and take it as normal; then, continue taking one tablet once a month on the scheduled days you've marked on your calendar.

If your next scheduled dose is more than 7 days away…
You should take one tablet the next morning after the day you remember; then, continue taking one tablet once a month on the scheduled days you've marked on your calendar.

Never take two Bondenza tablets within the same week.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Talk to a nurse or a doctor straight away if you notice any of the following serious side effects - you may need urgent medical treatment:

Common (may affect up to 1 in 10 people):
- flu-like symptoms, including fever, shaking and shivering, feeling of discomfort, bone pain and aching muscles and joints. Talk to a nurse or doctor if any effects become troublesome or last more than a couple of days
- rash. You may be having an allergic reaction to the medicine

Uncommon (may affect up to 1 in 100 people)
- severe pain in the chest, severe pain after swallowing food or drink, severe nausea, or vomiting, difficulty in swallowing. You may have a severe inflammation of your gullet/food pipe, possibly with sores or constriction of the gullet/food pipe

Rare (may affect up to 1 in 1000 people):
- itching, swelling of your face, lips, tongue and throat, with difficulty breathing.
- persistent eye pain and inflammation
- new pain, weakness or discomfort in your thigh, hip or groin. You may have early signs of a possible unusual fracture of the thigh bone

Very rare (may affect up to 1 in 10,000 people):
- pain or sore in your mouth or jaw, You may have early signs of severe jaw problems (necrosis (dead bone tissue) in the jaw bone)
- serious, potentially life-threatening allergic reaction

Other possible side effects

Common (may affect up to 1 in 10 people):
- headache
- heartburn, discomfort in swallowing, stomach or tummy pain (may be due to an inflammation of the stomach), indigestion, nausea, having diarrhoea (loose bowels)
- muscle cramps, stiffness of your joints and limbs

Uncommon (may affect up to 1 in 100 people)
- dizziness
- flatulence (farting, feeling bloated)
- back pain
- feeling tired and exhausted

Rare (may affect up to 1 in 1000 people):
- inflammation of the duodenum (first section of the bowel) causing stomach pain
- hives

If you get any of the side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

5. How to store Bondenza

Keep this medicine out of the sight and reach of children.

There are no special storage instructions.

Do not use this medicine after the expiry date which is stated on the carton after "EXP". The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Bondenza contains

- The active substance is ibandronic acid. One tablet contains 150 mg of ibandronic acid (as sodium monohydrate).
- The other ingredients are:

tablet core: lactose monohydrate, povidone, cellulose microcrystalline, crospovidone, stearic acid purified, silica colloidal anhydrous

tablet coat: hypromellose, titanium dioxide (E 171), talc, macrogol 6000

What Bondenza looks like and contents of the pack

Bondenza tablets are white to off white, of oblong shape and marked “BNVA” on one side, and “150” on the other side. The tablets are supplied in blisters containing 1 or 3 tablets.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Roche Registration Limited
6 Falcon Way
Shire Park
Welwyn Garden City
AL7 1TW
United Kingdom

Manufacturer
Roche Pharma AG
Emil-Barell-Strasse 1
D-79639 Grenzach-Wyhlen
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
N.V. Roche S.A.
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Luxembourg/Luxemburg
(Voir/siehe Belgique/Belgien)

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Slovenská republika
Roche Slovensko, s.r.o.
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Roche Products Ltd.
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This leaflet was last revised in {date}.

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

REMINDER STICKERS TEXT

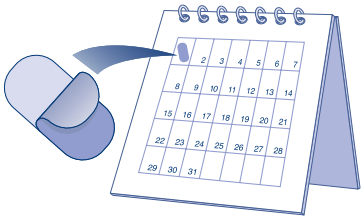
PLANNING WHEN TO TAKE BONDENZA

The dose of Bondenza is one tablet once a month. Choose one day of the month that will be easy to remember:

- either the same date (such as the 1st of each month)
- or the same day (such as the first Sunday of each month).

Use the peel-off stickers below to mark the dates on your calendar.

Once you've taken your tablet, put a tick in the box on the sticker.



PEEL-OFF STICKERS FOR YOUR PERSONAL CALENDAR

Monthly tablet	Monthly tablet	Monthly tablet
Bondenza	Bondenza	Bondenza

It's important to keep taking Bondenza every month.

Package leaflet: Information for the user

Bondenza 3 mg solution for injection
ibandronic acid

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

1. What Bondenza is and what it is used for

Bondenza belongs to a group of medicines called bisphosphonates. It contains the active substance ibandronic acid.
Bondenza may reverse bone loss by stopping more loss of bone and increasing bone mass in most women who take it, even though they won't be able to see or feel a difference. Bondenza may help lower the chances of breaking bones (fractures). This reduction in fractures was shown for the spine but not for the hip.

Bondenza 3 mg solution for injection in pre-filled syringes is a solution for intravenous injection by a health care professional. **Do not inject Bondenza yourself.**

Bondenza is prescribed to you to treat postmenopausal osteoporosis because you have an increased risk of fractures. Osteoporosis is a thinning and weakening of the bones, which is common in women after the menopause. At the menopause, a woman's ovaries stop producing the female hormone, oestrogen, which helps to keep her skeleton healthy. The earlier a woman reaches the menopause, the greater her risk of fractures in osteoporosis.

Other things that can increase the risk of fractures include:

- not enough calcium and vitamin D in the diet
- smoking cigarettes, or drinking too much alcohol
- not enough walking or other weight-bearing exercise
- a family history of osteoporosis

A healthy lifestyle will also help you to get the most benefit from your treatment. This includes:
- eating a balanced diet rich in calcium and vitamin D
- walking or other weight-bearing exercise
- not smoking and not drinking too much alcohol

2. What you need to know before you receive Bondenza

Do not receive Bondenza
- **if you have, or had in the past, low blood calcium**. Please consult your doctor
- if you are allergic to ibandronic acid or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Some patients need to be especially careful when using Bondenza. Talk to your doctor before receiving Bondenza:
- If you have or have ever had kidney problems, kidney failure or have needed dialysis, or if you have any other disease that may affect your kidneys
- If you have any disturbance of mineral metabolism (such as vitamin D deficiency)
- You should take calcium and vitamin-D supplements while receiving Bondenza. If you are unable to do so, you should inform your doctor
- If you are under dental treatment or will undergo dental surgery, tell your dentist that you are being treated with Bondenza.
- If you have heart problems and the doctor recommended to limit your daily fluid intake

Cases of serious, sometimes fatal, allergic reaction have been reported in patients treated with intravenous ibandronic acid. If you experience one of the following symptoms, such as shortness of breath/difficulty breathing, tight feeling in throat, swelling of tongue, dizziness, feeling of loss of consciousness, redness or swelling of face, body rash, nausea and vomiting, you should immediately alert your doctor or nurse (see section 4).

Children and adolescents
Bondenza must not be used in children or adolescents below 18 years.

Other medicines and Bondenza
Tell your doctor, nurse or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding
You should not be given Bondenza if you are pregnant, or if there is a possibility you may become pregnant. If you are breast-feeding, you will need to stop breast-feeding in order to receive Bondenza. Ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
You can drive and use machines as it's expected that Bondenza has no or negligible effect on your ability to drive and use machines.

Bondenza contains less than 1 mmol sodium (23 mg) per dose (3 ml), i.e. essentially "sodium-free".

3. How to receive Bondenza

The recommended dose of Bondenza for the intravenous injection is 3 mg (1 pre-filled syringe) once every 3 months.

The injection should be given into the vein by a physician or qualified/trained health care worker. Do not administer the injection to yourself.

The solution for injection must be administered into a vein only, and not anywhere else in the body.

Continuing to receive Bondenza
To get the most benefit from the treatment it is important to continue receiving the injections every 3 months for as long as your doctor prescribes it for you. Bondenza can treat osteoporosis only for as long as you keep receiving the treatment, even though you will not be able to see or feel a difference.

You should also take calcium and vitamin-D supplements, as recommended by your doctor.

If too much Bondenza is given
You may develop low levels of calcium, phosphorus or magnesium in the blood. Your doctor may take steps to correct such changes and may give you an injection containing these minerals.

If a dose of Bondenza is missed
You should arrange an appointment to get the next injection as soon as possible. After that, go back to getting the injections every 3 months from the date of the most recent injection.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Talk to a nurse or a doctor straight away if you notice any of the following serious side effects - you may need urgent medical treatment:

Common (may affect up to 1 in 10 people):
- flu-like symptoms, including fever, shaking and shivering, feeling of discomfort, fatigue, bone pain and aching muscles and joints. Talk to a nurse or doctor if any effects become troublesome or last more than a couple of days
- rash. You may be having an allergic reaction to the medicine

Rare (may affect up to 1 in 1000 people):
- itching, swelling of your face, lips tongue and throat, with difficulty breathing.
- persistent eye pain and inflammation (if prolonged)
- new pain, weakness or discomfort in your thigh, hip or groin. You may have early signs of a possible unusual fracture of the thigh bone.

Very rare (may affect up to 1 in 10000 people):
- pain or sore in your mouth or jaw. You may have early signs of severe jaw problems (necrosis (dead bone tissue) in the jaw bone).
- serious, potentially life-threatening allergic reaction (see section 2).

Other possible side effects

Common (may affect up to 1 in 10 people):
- headache
- stomach pain (such as gastritis) or tummy pain, , indigestion, nausea, having diarrhoea (loose bowels) or constipation
- pain in your muscles, joints, or back
- feeling tired and exhausted

Uncommon (may affect up to 1 in 100 people)
- inflammation of a vein
- pain or injury at the injection site
- bone pain
- feeling weak

Rare (may affect up to 1 in 1000 people):
- hives

If you get any of the side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

5. How to store Bondenza

Keep this medicine out of the sight and reach of children.

This medicinal product does not require any special storage conditions.

Do not use this medicine after the expiry date which is stated on the carton and on the syringe after "EXP". The expiry date refers to the last day of that month.

The person giving the injection should throw away any unused solution and put the used syringe and injection needle into an appropriate disposal container.

6. Content of the pack and other information

What Bondenza contains

- The active substance is ibandronic acid. One pre-filled syringe contains 3 mg of ibandronic acid in 3 ml of solution (as sodium monohydrate).
- The other ingredients are sodium chloride, acetic acid, sodium acetate trihydrate and water for injections.

What Bondenza looks like and contents of the pack

Bondenza 3 mg solution for injection in pre-filled syringes is a clear colourless solution. Each pre-filled syringe contains 3 ml of solution. Bondenza is available in packs of 1 pre-filled syringe and 1 injection needle or 4 pre-filled syringes and 4 injection needles.
Not all pack sizes may be marketed.

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This leaflet was last revised in {date}.

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu.

This information is intended for healthcare professionals only:

INFORMATION FOR THE HEALTHCARE PROFESSIONALS

Please see the Summary of Product Characteristics for more information.

Administration of Bondenza 3 mg solution for injection in pre-filled syringe:

Bondenza 3 mg solution for injection in pre-filled syringe should be injected intravenously over a period of 15 - 30 seconds.

The solution is irritant, therefore strict adherence to the intravenous route of administration is important. If you inadvertently inject into the tissues around the vein, patients may experience local irritation, pain and inflammation at the injection site.

Bondenza 3 mg solution for injection in pre-filled syringe **must not** be mixed with calcium-containing solutions (such as Ringer-Lactate solution, calcium heparin) or other intravenously administered medicinal products. Where Bondenza is administered via an existing intravenous infusion line, the intravenous infusate should be restricted to either isotonic saline or 50 mg/ml (5 %) glucose solution.

Missed dose:

If a dose is missed, the injection should be administered as soon as convenient. Thereafter, injections should be scheduled every 3 months from the date of the last injection.

Overdose:

No specific information is available on the treatment of overdosage with Bondenza.

Based on knowledge of this class of compounds, intravenous overdosage may result in hypocalcaemia, hypophosphataemia, and hypomagnesaemia, which can cause paraesthesia. In severe cases intravenous infusion of appropriate doses of calcium gluconate, potassium or sodium phosphate, and magnesium sulfate, may be needed.

General advice:

Bondenza 3 mg solution for injection in pre-filled syringe like other bisphosphonates administered intravenously, may cause a transient decrease in serum calcium values.

Hypocalcaemia and other disturbances of bone and mineral metabolism should be assessed and effectively treated before starting Bondenza injection therapy. Adequate intake of calcium and vitamin D is important in all patients. All patients must receive supplemental calcium and vitamin D.

Patients with concomitant diseases, or who use medicinal products which have a potential for undesirable effects on the kidney, should be reviewed regularly in line with good medical practice during treatment.

Any unused solution for injection, syringe and injection needle should be disposed of in accordance with local requirements.