AGRIPPAL® 2012

NAME OF MEDICINE

Inactivated Influenza Vaccine (surface antigen)

DESCRIPTION

Agrippal is a clear colourless suspension for injection. It is an egg-grown, inactivated influenza virus vaccine based on isolated surface antigens of A and B strains of influenza virus. The antigen composition and strains for the 2012 influenza season corresponds to the following types:

A/California/7/2009 (H1N1) – like strain (A/California/7/2009, NYMC X-181);

A/Perth/16/2009 (H3N2) – like strain (A/Victoria/210/2009, NYMC X-187); and

B/Brisbane/60/2008 – like strain (B/Brisbane/60/2008, NYMC BX-35)

The type and amount of viral antigens in Agrippal conform to the requirements of the Australian Influenza Vaccine Committee (AIVC) and the New Zealand Ministry of Health for the winter of 2012. The strains chosen for vaccine manufacture are endorsed by the AIVC as being antigenically equivalent to the reference virus.

Each 0.5 mL vaccine dose contains 15µg haemagglutinin of each of the recommended strains. The vaccine preparation also contains Sodium chloride 4.0 mg, Potassium chloride 0.1 mg, Potassium dihydrogen phosphate 0.1 mg, Sodium phosphate-dibasic 0.66 mg, Magnesium chloride 0.05 mg, Calcium chloride 0.06 mg and Water for Injections to 0.5 mL. The vaccine may contain residues of the following substances: eggs, chicken proteins, kanamycin sulfate, neomycin sulfate, sodium citrate, barium sulfate, formaldehyde, sucrose, cetrimonium bromide (CTAB), polysorbate 80 and less than 0.2 µg of ovalbumin per 0.5 mL dose.

PHARMACOLOGY

Agrippal induces humoral antibodies against haemagglutinins, the surface antigens of the virus. These antibodies neutralize influenza viruses and are important in the prevention of natural infections.

Seroprotection is generally obtained within 2 to 3 weeks. The duration of postvaccinal immunity to homologous strains or to strains closely related to the vaccine strains varies but is usually 6-12 months.

Influenza viral strains undergo antigenic changes from year to year. Therefore the antigen component of Agrippal is revised for every flu season and annual vaccination is recommended.

INDICATIONS

For the prevention of influenza caused by Influenza Virus, Types A and B.

For full details regarding the recommendations for influenza vaccination refer to the current NHMRC guidelines specified in the Australian Immunisation Handbook.

CONTRAINDICATIONS

Agrippal should not be administered to subjects with a known hypersensitivity to the active substance, to any of the excipients and to eggs, chicken proteins, kanamycin, neomycin, formaldehyde, barium sulfate, cetrimonium bromide (CTAB) or Polysorbate 80, or to anyone who has had an anaphylactoid reaction to a previous influenza vaccination.

Immunisation should be postponed in patients with an acute severe febrile illness (fever > 38.5°C). The presence of a minor illness with or without fever should not contraindicate use of Agrippal.

PRECAUTIONS

As with all injectable vaccines, appropriate medical treatment and supervision should always be readily available in case of a rare anaphylactic event following the administration of the vaccine.

The vaccine should under no circumstances be administered intravascularly.

Antibody response in patients with endogenous or iatrogenic immunosuppression may be insufficient.

Limited data is available in immunocompromised patients.

Patients with a history of Guillain-Barré Syndrome have a substantially greater likelihood of subsequently experiencing GBS than people without such a history. Thus, the likelihood of coincidentally experiencing GBS after influenza vaccination is expected to be greater in these patients than among people with no history of this syndrome. Whether influenza vaccination specifically might increase the risk for recurrence of GBS is unknown.

If GBS has occurred within 6 weeks of receipt of prior influenza vaccine, the decision to give Agrippal or any influenza vaccine should be based on careful evaluation of the potential benefits and possible risks.

Antibiotics (kanamycin sulfate and neomycin sulfate), and formaldehyde are also used during the manufacturing process and therefore trace amounts may be present in the final vaccine.

The syringe is for single use only and should not be used in more than one person.

Effects on Fertility

There were no effects on the mating performance or fertility of female rabbits in an embryofoetal and postnatal development study in which rabbits were intramuscularly injected with AGRIPPAL 35, 20 and 6 days prior to mating and on days 7 and 20 after mating (see also Use in Pregnancy).

Carcinogenicity and genotoxicity

AGRIPPAL has not been tested for carcinogenic or genotoxic potential.

Use in Pregnancy

Category B1.

There is no evidence of risk to the fetus from immunisation of pregnant women using inactivated virus vaccines, bacterial vaccines, or toxoids.

In an embryofoetal and post natal development study in rabbits intramuscularly injected with AGRIPPAL (15µg of each haemagglutinin antigen, i.e. the clinical dose) 35, 20 and 6 days prior to mating, and on gestation days 7 and 20, there were no significant toxicology effects in the dams, or their fetuses or pups. Anti-HA antibodies were detected in all vaccine-treated females, all their litters and in all but one pup.

Refer to the current edition of The Australian Immunisation Handbook for recommendations for use in pregnancy.

Use in Lactation

AGRIPPAL may be used during lactation, although there is no human data on use during lactation.

In an embryofoetal and post natal development study in rabbits, maternal treatment prior to mating and during gestation had no effects on pup development, assessed to lactation day 29 (see also Use in Pregnancy)

INTERACTIONS WITH OTHER MEDICINES

AGRIPPAL may be given at the same time as other vaccines. Immunisation should be carried out on separate limbs. It should be noted that the adverse reactions may be intensified.

The immunological response may be diminished if the patient is undergoing immunosuppressant treatment.

Influenza vaccine can impair the metabolism of warfarin, theophylline, phenytoin, phenobarbitone and carbamazepine by the hepatic P450 system. Results from studies have been variable in degree of interaction and time after vaccination for the interaction to take effect. The interaction may be idiosyncratic. Patients taking warfarin, theophylline, phenytoin, phenobarbitone or carbamazepine should be advised of the possibility of an interaction and told to look out for signs of elevated levels of medication.

Effect on Laboratory Tests

Following influenza vaccination, false positive results in serology tests using the ELISA method to detect antibodies against HIV1, Hepatitis C and especially HTLV1 have been observed. The Western Blot technique disproves the results. The transient false positive reactions could be due to the IgM response by the vaccine.

ADVERSE EFFECTS

The safety of trivalent inactivated influenza vaccines is assessed in open label, uncontrolled clinical trials performed as annual update requirement, including at least 50 adults aged 18 – 60 years of age and at least 50 elderly aged 61 years or older. Safety evaluation is performed during the first 3 days following vaccination.

The following undesirable effects have been observed during clinical trials with the following frequencies:

Very common (≥1/10); common (≥1/100, <1/10); uncommon (≥1/1,000, <1/100); rare (≥1/10,000, <1/1,000); very rare (<1/10,000), including isolated reports.

Nervous system disorders
Common: Headache*

Skin and subcutaneous tissue disorders
Common: Sweating*

Musculoskeletal and connective tissue disorders
Common: Myalgia, arthralgia*

General disorders and administration site conditions
Common: Fever, malaise, shivering, fatigue.
Local reactions: redness, swelling, pain, ecchymosis, induration.*

*These reactions usually disappear within 1-2 days without treatment.

Adverse Reactions reported from Post Marketing Surveillance

Adverse reactions reported from post marketing surveillance are, next to the reactions which have also been observed during the clinical trials, the following:

Blood and lymphatic system disorders:
Thrombocytopenia (some very rare cases were severe with platelet counts less than 5,000 per mm^3), lymphadenopathy

Immune system disorders:
Allergic reactions, in rare cases leading to shock, angioedema

Nervous system disorders:
Neuralgia, paraesthesiae, febrile convulsions, neurological disorders, such as encephalomyelitis, neuritis and Guillain-Barré syndrome

Vascular disorders:
Vasculitis associated in very rare cases with transient renal involvement

Skin and subcutaneous tissue disorders:
Generalised skin reactions including pruritus, urticaria or non-specific rash

DOSAGE AND ADMINISTRATION

Adults and children from 36 months: 0.5 mL.

Children 6 months to 35 months of age: 0.25 mL.

For children less than 9 years of age who are receiving influenza vaccine for the first time, a second dose is recommended after an interval of at least 4 weeks.

Immunisation should be carried out by intramuscular injection.

Use once only in one patient and discard any residue.

Instructions for use and handling

Unused vaccine and other waste material should be disposed of in compliance with local rules for the disposal of products of this nature.

The vaccine should be allowed to reach room temperature before use.

Shake before use.

If half a dose (0.25 ml) is to be administered, discard half the contained volume (up to the mark indicated on the syringe barrel), before injection.

Inspect Agrippal visually for the presence of particulate matter or discoloration prior to administration, whenever suspension and container permit. If either of these conditions exists, do not use the contents.

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

OVERDOSAGE

Overdosage is unlikely to have any untoward effect. For general advice on overdose management in Australia, contact the Poisons Information Centre on 13 11 26.

PRESENTATION AND STORAGE CONDITIONS

Presentation

Each pre-filled syringe (type I glass) contains a 0.5 mL dose of vaccine. Packs of 1 or 10 with needle (AUST R: 144670).

A pack without needle is also registered (AUST R 177605) but is currently not marketed.

Storage conditions

Store refrigerated between 2°C - 8°C. Do not freeze. Store in the original package in order to protect from light.

NAME AND ADDRESS OF THE SPONSOR

Novartis Vaccines and Diagnostics Pty. Ltd
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POISON SCHEDULE OF THE MEDICINE

All states and ACT: S4

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAEUTIC GOODS (the ARTG)

Date of first TGA Approval: 16 February 2009

DATE OF MOST RECENT AMENDMENTS

Date of Safety Related Amendment: 09 November 2010
Date of Strain Update: 10 December 2010

Date of Safety Related Notification: 01 August 2011
Date of Strain Update: 21 November 2011
Date of Safety Related Notification: 12 October 2012

Product Information (PI) and Consumer Medicine Information (CMI) documents are regularly updated.

Please also refer to the TGA web site (https://www.ebs.tga.gov.au) for the most up to date PI and CMI.

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